

891 S2
 203462 LYSOSOM?
 S3 85 S2 (S) LYSOSOM?
 ? s s2 and review
 891 S2
 5627900 REVIEW
 S4 61 S2 AND REVIEW
 ? show files;ds;t/3,k/all
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S1	2338	ANTIBOD? (S) DELIVER? (S) INTRACELL?
S2	891	RD (unique items)
S3	85	S2 (S) LYSOSOM?
S4	61	S2 AND REVIEW

>>>KWIC option is not available in file(s): 399

4/3,K/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
 (c) 2005 BIOSIS. All rts. reserv.

0014870989 BIOSIS NO.: 200400239936
 Influenza virus: Immunity and vaccination strategies. Comparison of the
 immune response to inactivated and live, attenuated influenza vaccines.
 AUTHOR: Cox R J (Reprint); Brokstad K A; Ogra P
 AUTHOR ADDRESS: Influenza Research Centre, The Gade Institute, University
 of Bergen, Bergen High Technology Centre, N-5020, P.O. Box 7800, Bergen,
 Norway**Norway
 AUTHOR E-MAIL ADDRESS: rebecca.cox@mbi.uib.no
 JOURNAL: Scandinavian Journal of Immunology 59 (1): p1-15 January 2004
 2004
 MEDIUM: print
 ISSN: 0300-9475 _(ISSN print)
 DOCUMENT TYPE: Article
 RECORD TYPE: Abstract
 LANGUAGE: English

...ABSTRACT: of influenza, and the mucosal immune system provides the first
 line of defence against infection. Secretory immunoglobulin A (SIgA) and
 IgM are the major neutralizing **antibodies** directed against mucosal
 pathogens. These *****antibodies***** work to prevent pathogen entry and can
 function *****intracellularly***** to inhibit replication of virus. This
review describes influenza virus infection, epidemiology, clinical
 presentation and immune system response, particularly as it pertains to
 mucosal immunity and vaccine use. Specifically, this *****review*****
 provides an update of the current status on influenza vaccination and
 concentrates on the two main types of influenza vaccines currently in
 use, namely the cold-adapted vaccine (CAV) given intranasally/orally, and
 the inactivated vaccine (IV) **delivered** subcutaneously or
 intramuscularly. The commercially available trivalent IV (TIV) elicits
 good serum **antibody** responses but induces poorly mucosal IgA
*****antibody***** and cell-mediated immunity. In contrast, the CAV may
 elicit a long-lasting, broader immune (humoral and cellular) response,

which more closely resembles natural immunity. The immune response induced by these two vaccines will be compared in this ***review*** .

4/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014609081 BIOSIS NO.: 200300567800
Targeting dendritic cells for priming cellular immune responses.
AUTHOR: Gogolak Peter; Rethi Bence; Hajas Gyorgy; Rajnavolgyi Eva (Reprint)
AUTHOR ADDRESS: 98 Nagyerdei Blvd, Debrecen, H-4012, Hungary**Hungary
AUTHOR E-MAIL ADDRESS: evaraj@jaguar.dote.hu
JOURNAL: Journal of Molecular Recognition 16 (5): p299-317
September-October 2003 2003
MEDIUM: print
ISSN: 0952-3499 (ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: particles carrying such structures and apoptotic or necrotic cells. This process is facilitated by specialized receptors with high endocytic capacity, which provides potential targets for **delivering** designed molecules. The best route for targeting B- and/or T cell epitopes, however, is still the subject of intense investigation. Immature DC, which reside...

...to draining lymph nodes where they act as highly potent professional antigen presenting cells. This is brought about by the ability to present their accumulated **intracellular** content for both CD4+ helper (Th) and CD8+ cytotoxic/cytolytic T lymphocytes (Tc/CTL). Engulfed proteins are processed **intracellularly** and their peptide fragments are transported to the cell surface in the context of major histocompatibility complex encoded class I and II molecules for presentation...


...support the interaction of DC with T lymphocytes, and the cytokines secreted by DC, which polarize immune responses to Th1-mediated cellular or Th2-mediated ***antibody*** responses. These results altogether demonstrate that monocyte-derived DC are useful candidates for in vitro or in vivo targeting of antigens to induce efficient adaptive...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014528154 BIOSIS NO.: 200300485811
Intracellular antibodies and challenges facing their use as therapeutic agents.
AUTHOR: Lobato M Natividad; Rabbitts Terence H (Reprint)
AUTHOR ADDRESS: MRC Laboratory of Molecular Biology, Hills Road, Cambridge, CB2 2QH, UK**UK
AUTHOR E-MAIL ADDRESS: thr@mrc-lmb.cam.ac.uk
JOURNAL: Trends in Molecular Medicine 9 (9): p390-396 September 2003 2003
MEDIUM: print
ISSN: 1471-4914 (ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English



ABSTRACT: A key feature of **antibodies** is their ability to bind antigens with high specificity and affinity. This has led to the concept of **intracellular antibodies** (intrabodies), designed to mimic *****antibody***** -antigen binding, but inside cells. *****Antibody***** fragments comprising the antigen-binding variable domains are convenient formats for intrabodies, potentially allowing for **intracellular** functionality. Intrabodies are promising tools, capable of interfering with a wide range of molecular targets in various **intracellular** compartments. However, many significant challenges remain to be overcome before intrabodies can be useful therapeutic agents. Although major progress has been made in the design and selection of intrabodies, new developments and advances are needed to allow their efficient *****delivery***** and expression for treatment of human diseases.

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature *****Review*****

4/3,K/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014361501 BIOSIS NO.: 200300320220

Targeting ICAM-1/LFA-1 interaction for controlling autoimmune diseases:

Designing peptide and small molecule inhibitors.

AUTHOR: Anderson Meagan E; Siahaan Teruna J (Reprint)

AUTHOR ADDRESS: Department of Pharmaceutical Chemistry, University of Kansas, 2095 Constant Avenue, Lawrence, KS, 66047, USA**USA

AUTHOR E-MAIL ADDRESS: siahaan@ku.edu

JOURNAL: Peptides (New York) 24 (3): p487-501 March 2003 2003

MEDIUM: print

ISSN: 0196-9781

DOCUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: This **review** describes the role of modulation of **intracellular** adhesion molecule-1 (ICAM-1)/leukocyte function-associated antigen-1 (LFA-1) interaction in controlling autoimmune diseases or inducing immunotolerance. ICAM-1/LFA-1 interaction ...

...cells to target tissues. This interaction also functions, along with Signal-1, as a co-stimulatory signal (Signal-2) for T-cell activation, which is **delivered** by the T-cell receptors (TCR)-major histocompatibility complex (MHC)-peptide complex. Therefore, blocking ICAM-1/LFA-1 interaction can suppress T-cell activation in autoimmune diseases and organ transplantation. Many types of inhibitors (i.e. **antibodies**, peptides, small molecules) have been developed to block ICAM-1/LFA-1 interactions, and some of these molecules have reached clinical trials. Peptides derived from...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature *****Review*****

4/3,K/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0014266756 BIOSIS NO.: 200300225475

Immunological hurdles to lung gene therapy.

AUTHOR: Ferrari S (Reprint); Griesenbach U; Geddes D M; Alton E

AUTHOR ADDRESS: Department of Gene Therapy, Faculty of Medicine, National

Heart and Lung Institute, Imperial College, London, SW3 6LR, UK**UK
AUTHOR E-MAIL ADDRESS: stefano.ferrari@ulss12.ve.it
JOURNAL: Clinical and Experimental Immunology 132 (1): p1-8 April 2003
2003
MEDIUM: print
ISSN: 0009-9104 (ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Gene **delivery** has the potential to offer effective treatment to patients with life-threatening lung diseases such as cystic fibrosis, alphas-1-antitrypsin deficiency and lung cancer. Phase...

...trials have shown that, in principle, gene transfer to the lung is feasible and safe. However, gene expression from both viral and non-viral gene *****delivery***** systems has been inefficient. In addition to extra- and **intracellular** barriers, the host innate and acquired immune system represents a major barrier to successful gene transfer to the lung. Results from studies in experimental animals and clinical trials have shown that inflammatory, **antibody** and T cell responses can limit transgene expression duration and readministration of the gene transfer vector. We will *****review***** here how the development of pharmacological and/or immunological agents can modulate the host immune system and the limitations of these strategies. A better understanding...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature *****Review*****

4/3,K/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013347801 BIOSIS NO.: 200100519640
Protein-protein interactions in hematology and phage display
AUTHOR: Mullaney Brian P (Reprint); Pallavicini Maria G
AUTHOR ADDRESS: Myriad Genetic Laboratories, 320 Wakara Way, Salt Lake City, UT, 84108, USA**USA
JOURNAL: Experimental Hematology (Charlottesville) 29 (10): p1136-1146
October, 2001 2001
MEDIUM: print
ISSN: 0301-472X
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Phage display, which exploits fundamental tools and principles of immune repertoire diversity, antigen-**antibody** interactions, and clonal and immunologic selection, is used increasingly to advance experimental and clinical hematology. Phage display is based on the ability of bacteriophage to present engineered proteins on their surface coat. Diverse libraries of proteins such as peptides, *****antibody***** fragments, and protein domains corresponding to gene fragments or cDNAs may be displayed. Interactions between phage-displayed proteins and target antigens can be identified rapidly...

...and gene fragment libraries are particularly useful to characterize binding interactions between proteins, such as ligand-receptor interactions. This approach allows rapid generation of human *****antibodies*****, often against nonimmunogenic, conserved proteins. Phage **antibodies** against surface and **intracellular** antigens are used as reagents for flow cytometry, in vivo imaging, and therapeutic targeting. Phage-derived *****antibodies***** also facilitate analyses of the

humoral ***antibody*** response. Finally, cellular ***delivery*** of phage-displayed peptides and gene fragments can be used to modulate functional pathways and molecules in vitro and in vivo. The combinatorial power of...

...high-throughput approach to develop tools and reagents useful for a plethora of experimental hematology applications. This paper focuses on current and future applications of **antibody** and epitope phage display technology in hematology.

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013169130 BIOSIS NO.: 200100340969

Revealing the potential of DNA-based vaccination: Lessons learned from the hepatitis B virus surface antigen

AUTHOR: Schirmbeck Reinhold (Reprint); Reimann Joerg

AUTHOR ADDRESS: Institute for Medical Microbiology and Immunology,
University of Ulm, D-89081, Ulm, Germany**Germany

JOURNAL: Biological Chemistry 382 (4): p543-552 April, 2001 2001

MEDIUM: print

ISSN: 1431-6730

DOCUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: DNA-based vaccination is a novel technique to efficiently stimulate humoral (**antibody**) and cellular (T cell) immune responses to protein antigens. In DNA-based vaccination, immunogenic proteins are expressed in in vivo transfected cells of the vaccine recipients in their native conformation with correct posttranslational modifications from antigen-encoding expression plasmid DNA. This ensures the integrity of **antibody**-defined epitopes and supports the generation of protective (neutralizing) ***antibody*** titers. Plasmid DNA vaccination is furthermore an exceptionally potent strategy to stimulate CD8+ cytotoxic T lymphocyte (CTL) responses because antigenic peptides are efficiently generated by endogenous processing of **intracellular** protein antigens. These key features make DNA-based immunization an attractive strategy for prophylactic and therapeutic vaccination against extra- and ***intracellular*** pathogens. In this brief ***review***, we summarize the current state of expression vector design, DNA **delivery** strategies, priming immune responses to **intracellular** or secreted antigens by DNA vaccines and unique advantages of DNA- versus recombinant protein-based vaccines using the hepatitis B surface antigen (HBsAg) as a

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0012473062 BIOSIS NO.: 200000191375

Molecular engineering of proteins and polymers for targeting and intracellular delivery of therapeutics

AUTHOR: Stayton Patrick S (Reprint); Hoffman Allan S; Murthy Niren; Lackey Chantal; Cheung Charles; Tan Philip; Klumb Lisa A; Chilkoti Ashutosh; Wilbur F Scott; Press Oliver W

AUTHOR ADDRESS: Department of Bioengineering, University of Washington,
Seattle, WA, 98195, USA**USA
JOURNAL: Journal of Controlled Release 65 (1-2): p203-220 March 1, 2000
2000
MEDIUM: print
ISSN: 0168-3659
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: There are many protein and DNA based therapeutics under development in the biotechnology and pharmaceutical industries. Key **delivery** challenges remain before many of these biomolecular therapeutics reach the clinic. Two important barriers are the effective targeting of drugs to specific tissues and cells and the subsequent *****intracellular***** *****delivery***** to appropriate cellular compartments. In this **review**, we summarize protein engineering work aimed at improving the stability and refolding efficiency of **antibody** fragments used in targeting, and at constructing new streptavidin variants which may offer improved performance in pre-targeting *****delivery***** strategies. In addition, we *****review***** recent work with pH-responsive polymers that mimic the membrane disruptive properties of viruses and toxins. These polymers could serve as alternatives to fusogenic peptides in gene therapy formulations and to enhance the **intracellular delivery** of protein therapeutics that function in the cytoplasm.

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature *****Review*****

4/3,K/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0011716390 BIOSIS NO.: 199800510637
Genetically engineered antibodies in gene transfer and gene therapy
AUTHOR: Pelegrin Mireia; Marin Mariana; Noel Daniele; Piechaczyk Marc
(Reprint)
AUTHOR ADDRESS: Inst. Molecular Genetics Montpellier, CNRS, UMR 5535/IFR
24, 1919 Route Mende, 34293 Montpellier Cedex 05, France**France
JOURNAL: Human Gene Therapy 9 (15): p2165-2175 Oct. 10, 1998 1998
MEDIUM: print
ISSN: 1043-0342
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Our ability to produce and engineer human monoclonal **antibodies** provides a basis for the development of novel therapeutical strategies against a variety of diseases. These strategies not only include improved passive immunotherapy but also more sophisticated **antibody**-based gene therapies involving gene transfer approaches. Four of the major applications of *****antibody***** gene engineering in the field of gene therapy are reviewed here. These are (1) the redefinition of viral vector tropism of infection for better transduction...

...recognition activities to effector cells of the immune system to kill cancer and pathogen-infected cells, (3) the inhibition of cellular and viral functions through **intracellular** expression of **antibody**-derived molecules, and (4) the systemic **delivery** of therapeutic monoclonal *****antibodies***** by non-B cells in living organisms.

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0011701652 BIOSIS NO.: 199800495899
Receptor-mediated delivery of plasmid DNA
AUTHOR: Wagner E (Reprint)
AUTHOR ADDRESS: Inst. Biochem., Vienna Univ. Biocenter, A-1030 Vienna,
Austria**Austria
JOURNAL: Biogenic Amines 14 (5): p519-536 1998 1998
MEDIUM: print
ISSN: 0168-8561
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A goal in gene therapy is the **delivery** of genes to the surface of the target cells, followed by an efficient uptake and transport across ***intracellular*** barriers into the nucleus of cells. Amongst other systems, DNA/polycation particles coated with cell-binding ("targeting") ligands such as transferrin, EGF, asialoglycoprotein receptor binding molecules, or various **antibodies** are being optimized for this purpose. To allow ionic binding to the DNA, in most cases ligands are covalently linked to the polycations polylysine or...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0009570330 BIOSIS NO.: 199598038163
Targeting enzymes for cancer therapy: Old enzymes in new roles
AUTHOR: Deonarain M P (Reprint); Epenetos A A
AUTHOR ADDRESS: Tumour Targeting Lab., ICRF Oncol. Unit, Royal Postgraduate Med. Sch., Hammersmith Hosp., Du Cane Road, London W12 0HS, UK**UK
JOURNAL: British Journal of Cancer 70 (5): p786-794 1994 1994
ISSN: 0007-0920
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: enhance their activity in turnouts. These prodrug activation systems require the pretargeting of the enzyme to the surface of a tumour cell, usually by an ***antibody*** or its immunoreactive fragment. A recent novel approach proposes the **intracellular delivery** of appropriate enzymes, such as phosphodiesterases, to particular cellular compartments. There, enzyme activity can cause substantive damage resulting in cell death. Cell targeting of mammalian...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0009286953 BIOSIS NO.: 199497308238
Immunoliposome-mediated delivery of nucleic acids: A **review** of our

laboratory's experience

AUTHOR: Leserman Lee (Reprint); Machy Patrick; Zelphati Olivier

AUTHOR ADDRESS: Cent. Immunologie INSERM-CNRS, Marseille-Luminy, Case 906,
13288 Marseille Cedex 9, France**France

JOURNAL: Journal of Liposome Research 4 (1): p107-119 1994 1994

ISSN: 0898-2104

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Immunoliposome-mediated delivery of nucleic acids: A **review** of our
laboratory's experience

ABSTRACT: Experiments performed in our laboratory or in collaboration with
other groups demonstrating the **delivery** to cells of mono-, oligo-
and polynucleotides from **antibody**-targeted small liposomes are
reviewed. Biologically-active molecules *****delivered***** into cells via
these liposomes include: phosphorylated derivatives of dideoxyuridine,
which have activity against the human immunodeficiency virus; the
oligonucleotide (2'-5') (A)-n and...

...the RNA duplex poly (rI:rC), and related molecules, which are inducers
of interferon and other cytokines; long RNA antisense molecules and
plasmids. Advantages for *****delivery***** by liposomes, as compared to use
of the same molecules free in solution include: protection against
degradation, reduction of toxicity, improved pharmacokinetics and the
possibility of increased *****intracellular***** transport. Numerous
parameters are important in determining if and to what extent liposome
contents are **delivered** to their sites of action, including:
liposome size, lipid composition, nature of the encapsulated molecule,
type of ligand used for targeting and its linkage to...

4/3,K/13 (Item 13 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0009263699 BIOSIS NO.: 199497284984

Understanding the CD4 molecule: Surface expression and function

AUTHOR: Morrison W J (Reprint); Offner H; Vandenbark A A

AUTHOR ADDRESS: Veterans Administration Med. Cent. 151-DD, 3710 SW US
Veterans Hospital Rd., Portland, OR 97207, USA**USA

JOURNAL: Journal of Neuroscience Research 38 (1): p1-5 1994 1994

ISSN: 0360-4012

DOCUMENT TYPE: Article; Literature Review

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: a receptor for human immunodeficiency virus (HIV)-gp120
glyco-protein. Both antigen-stimulated TCR activation and HIV infectivity
can be blocked by whole anti-CD4 *****antibodies*****. Although selective
modulation of CD4 from the surface by gangliosides (GM1) blocks HIV
infectivity, it enhances associated TCR function. Enhanced TCR function
has also been observed after **intracellular delivery** of
synthetic CD4 mRNA-antisense oligodeoxynucleotide (ODN) that block de
novo synthesis of CD4. These specific CD4 modulations were
mechanistically different from one another yet...

...the TCR. The proposed role of CD4 during TCR function and HIV
infectivity was developed, in part, according to decreases following CD4
antagonism by whole **antibody** or down-modulation of CD4 by
phorbol-stimulated protein kinase C activity. Selective CD4 modulations
have independently redefined the specific contributions of CD4 surface
expression...

DESCRIPTORS:

MISCELLANEOUS TERMS: ...Literature ***Review***

4/3,K/14 (Item 1 from file: 8)
DIALOG(R)File 8:Ei Compendex(R)
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07154724 E.I. No: EIP04508712403

Title: Virosomes for antigen and DNA delivery
Author: Daemen, Toos; De Mare, Arjan; Bungener, Laura; De Jonge, Jorgen;
Huckriede, Anke; Wilschut, Jan
Source: Advanced Drug Delivery Reviews v 57 n 3 SPEC. ISS. Jan 10 2005. p
451-463
Publication Year: 2005
CODEN: ADDREP ISSN: 0169-409X
Language: English

Abstract: Specific targeting and **delivery** as well as the display of
antigens on the surface of professional antigen-presenting cells (APCs) are
key issues in the design and development of...

...Prophylactic vaccination against infectious diseases in general aims at
the induction of humoral immune responses to prevent infection. This
humoral immune response is mediated by ***antibody*** -producing B cells.
On the other hand, therapeutic immunisation against virally infected cells
and tumour cells requires the induction of cytotoxic T lymphocytes (CTLs)
that...

...antigens within APCs, for example, after immunisation with live
attenuated virus. However, immunisation with live vaccines bears the risk
of causing disease. Therefore, alternative vaccine ***delivery*** systems,
which enable introduction of nonreplicating antigen into the MHC class I
presentation pathway, are sought. Furthermore, for the induction of
effective humoral and cellular responses, MHC class II restricted
activation of T helper cells (Th cells) is required. Among other
delivery systems, as described in this theme issue of Advanced Drug
Delivery Reviews, virosomes seem ideally suited for **delivery** of
antigens into both MHC pathways. In this ***review***, we will focus on
the use of virosomes as carrier vehicles for the **intracellular**
delivery of protein antigens and DNA, and the induction of a
cellular immune response against encapsulated protein antigens and
proteins expressed by virosome-associated plasmids. copy...

4/3,K/15 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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11002332 Genuine Article#: 596DJ No. References: 93

Title: Folate-mediated delivery of macromolecular anticancer therapeutic
agents

Author(s): Lu YJ; Low PS (REPRINT)

Corporate Source: Purdue Univ, Dept Chem, 1393 Borwn Bldg/W
Lafayette//IN/47907 (REPRINT); Purdue Univ, Dept Chem, W
Lafayette//IN/47907

Journal: ADVANCED DRUG DELIVERY REVIEWS, 2002, V54, N5 (SEP 13), P675-693
ISSN: 0169-409X Publication date: 20020913
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

...Abstract: exist where folate targeting has significantly improved the
outcome of a macromolecule-based therapy, leading to complete cures of
established tumors in many cases. This ***review*** presents a brief

mechanistic background of folate-targeted macromolecular therapeutics and then summarizes the successes and failures observed with each major application of the technology...

...Identifiers-- ***INTRACELLULAR*** DRUG- ***DELIVERY*** ; LIGAND-
ANTIBODY CONJUGATE; GPI-ANCHORED PROTEINS; RECEPTOR-TYPE-BETA;
CULTURED KB CELLS; BINDING-PROTEIN; OVARIAN-CANCER; GENE **DELIVERY**
; TUMOR-CELLS; IN-VIVO

4/3,K/16 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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10181261 Genuine Article#: 493XU No. References: 94
Title: Heat shock proteins: novel therapeutic tools for HIV-infection?
Author(s): Brenner BG (REPRINT) ; Wainberg Z
Corporate Source: McGill Univ,Jewish Gen Hosp, Lady Davis Inst,3755 Cote
Ste Catherine Rd/Montreal/PQ H3T 1E2/Canada/ (REPRINT); McGill
Univ,Jewish Gen Hosp, Lady Davis Inst,Montreal/PQ H3T 1E2/Canada/
Journal: EXPERT OPINION ON BIOLOGICAL THERAPY, 2001, V1, N1 (JAN), P67-77
ISSN: 1471-2598 Publication date: 20010100
Publisher: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE
FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

Abstract: Heat shock proteins (Hsps), cyclophilins (Cyps) and FK binding
proteins (FKBPs) form a family of **intracellular** chaperone
molecules that facilitate protein folding and assembly. These stress
proteins are selectively expressed in cells in response to a range of
stimuli, including heat, lymphokine and microbial/viral infections.
This **review** discusses the role of stress proteins in the HIV-1
viral life cycle, with regard to the development of specific Hsp-based
therapeutic strategies against...

...HIV-1 replication and infection, providing novel HIV-1 therapeutic
strategies. Moreover, Hsp binding to viral complexes can enhance
antiviral immunity, including natural killer (NK), **antibody**
-dependent (ADCC), gamma delta T-cell and cytotoxic T-lymphocyte (CTL)
activities against HIV-1 infected cells. The ability of Hsps to
interact with HIV-1 viral proteins, combined with their inherent
adjuvant and immunogenic properties indicates that Hsps may also serve
as vehicles for antigen *****delivery***** and the design of AIDS vaccines.

4/3,K/17 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.

09556316 Genuine Article#: 420VQ No. References: 321
Title: Ligand-receptor-mediated drug delivery: An emerging paradigm in
cellular drug targeting
Author(s): Vyas SP (REPRINT) ; Singh A; Sihorkar V
Corporate Source: Dr HS Gour Vishwavidyalaya,Drug Delivery Res Lab, Dept
Pharmaceut Sci,Sagar 470003/MP/India/ (REPRINT); Dr HS Gour
Vishwavidyalaya,Drug Delivery Res Lab, Dept Pharmaceut Sci,Sagar
470003/MP/India/; Panacea Biotech,Lalru/Punjab/India/
Journal: CRITICAL REVIEWS IN THERAPEUTIC DRUG CARRIER SYSTEMS, 2001, V18,
N1, P1-76
ISSN: 0743-4863 Publication date: 20010000
Publisher: BEGELL HOUSE INC, 79 MADISON AVE, SUITE 1205, NEW YORK, NY
10016-7892 USA
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

Abstract: Receptor-mediated cellular events have received major attention

in the field of drug/gene *****delivery***** in the past few years. These events, which are mediated through the endogenous ligands/epitopes, could be exploited for designing site-specific: and target-oriented *****delivery***** systems. The past decade has seen the development of endogenous ligands and their mimics of exogenous origins to selectively **deliver** the contained or immobilized moieties to the cellular interiors using a wide range of cell surface receptors/epitopes. Ligand-mediated active targeting has emerged as a novel paradigm in targeting either vascular compartment (first-order), cellular (second-order), or *****intracellular***** (third-order) levels. Most carrier systems or bioconjugates explored so far can be used as cargo units for the site-specific presentation and **delivery** of various bioactives using biorelevant ligands, including **antibodies**, polypeptides, oligosaccharides (carbohydrates), viral proteins, fusogenic; residues, and molecules of endogenous origin. In this **review** we describe various ligand-receptor systems that have been investigated to date for targeted or cellular drug *****delivery*****. These include blood carbohydrate (lectin) receptors, Fc receptors, complement receptors, interleukin receptors, lipoprotein receptors, transferrin receptors, scavenger receptors, receptors/epitopes expressed on tumor cells, and cell adhesion receptors. The role of receptors as molecular target has opened new opportunities for cellular or **intracellular** targeting using carrier systems appended with targeting handles (ligands). Research in the field of ligand-receptor-based targeted system is expected to be an armamentarium...

4/3,K/18 (Item 4 from file: 34)
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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08142782 Genuine Article#: 251EG No. References: 64
 Title: DNA vaccines: Basic mechanism and immune responses (**Review**)
 Author(s): Robinson HL (REPRINT)
 Corporate Source: YERKES REG PRIMATE RES CTR, 954 GATEWOOD
 NE/ATLANTA//GA/30329 (REPRINT)
 Journal: INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, 1999, V4, N5 (NOV), P 549-555
 ISSN: 1107-3756 Publication date: 19991100
 Publisher: PROFESSOR D A SPANDIDOS, 1, S MERKOURI ST, EDITORIAL OFFICE, ATHENS 116 35, GREECE
 Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

Title: DNA vaccines: Basic mechanism and immune responses (**Review**)
 Abstract: DNA vaccines raise immune responses by expressing proteins in vaccinated hosts. Responses are raised by nanogram levels of protein expression. Popular methods of DNA *****delivery***** include intramuscular (i.m.) injections of DNA in saline and gene gun *****delivery***** of DNA-coated gold beads to the epidermis. Professional antigen-presenting cells derived from the bone marrow present DNA-expressed antigens to T-cells. Following...
 ...transfected dendritic cells present antigens, whereas following i.m. immunizations both directly transfected dendritic cells and macrophages can present antigen. For both methods of DNA *****delivery*****, non-lymphoid cells can serve as factories of antigen for professional antigen presenting cells. Gene gun immunizations depend on antigen expression at the skin target...
 ...independent of DNA expression in the muscle target. For both methods, antigen expression capable of initiating an immune response persists for about one month. Intramuscular *****deliveries***** of DNA tend to raise type 1 T-cell help for **intracellular** and plasma membrane

antigens but type 2 T-cell help for secreted antigens. Gene gun immunizations tend to raise type 2 T-cell help for...

...and secreted antigens. In mice, DNA-raised immune responses can be equivalent to those raised by viral infections for both the height and longevity of ***antibody*** and cytotoxic T-cell responses.

4/3,K/19 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.

07720547 Genuine Article#: 200UJ No. References: 264
Title: Advances in cancer gene therapy
Author(s): Bilbao G; Contreras JL; Curiel DT (REPRINT)
Corporate Source: UNIV ALABAMA, GENE THERAPY CTR, 1824 6TH AVE S, WTI 620/BIRMINGHAM//AL/35294 (REPRINT); UNIV ALABAMA, GENE THERAPY CTR/BIRMINGHAM//AL/35294; UNIV ALABAMA, DEPT SURG/BIRMINGHAM//AL/35294; UNIV ALABAMA, DEPT PULM & CRIT CARE MED/BIRMINGHAM//AL/35294
Journal: EXPERT OPINION ON THERAPEUTIC PATENTS, 1999, V9, N6 (JUN), P 711-736
ISSN: 1354-3776 Publication date: 19990600
Publisher: ASHLEY PUBL LTD, 1ST FL, THE LIBRARY, 1 SHEPHERDS HILL HIGHGATE, LONDON N6 5QJ, ENGLAND
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

...Abstract: gene therapy has emerged as a new method of therapeutic and possibly preventive intervention against cancer targeted at the level of cellular gene expression. This ***review*** highlights current strategies and significant developments being employed in gene therapy for neoplastic diseases. Three main approaches currently being investigated are mutation compensation, molecular chemotherapy, and genetic immunotherapy. Mutation compensation relies on strategies to ablate activated oncogenes at the level of DNA (triplex), messenger RNA (antisense or ribozyme) or protein (**intracellular** single chain ***antibodies***), and augment tumour suppressor gene expression. Molecular chemotherapy uses the **delivery** of a toxin gene to tumour cells for eradication. This can be accomplished by either transductional targeting, whereby the toxin is specifically **delivered** to the tumour, or by transcriptional targeting, whereby tumour specific transcriptional activators are employed to selectively 'turn on' the toxin gene exclusively within the tumour...

4/3,K/20 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.

07258113 Genuine Article#: 142FC No. References: 94
Title: Molecular requirements for lineage commitment in the thymus - antibody-mediated receptor engagements reveal a central role for lck in lineage decisions
Author(s): Bommhardt U; Mee PJ; Tybulewicz VLJ; Zamoyska R (REPRINT)
Corporate Source: NATL INST MED RES, DIV MOL IMMUNOL, THE RIDGEWAY, MILL HILL/LONDON NW7 1AA//ENGLAND/ (REPRINT); NATL INST MED RES, DIV MOL IMMUNOL/LONDON NW7 1AA//ENGLAND/
Journal: IMMUNOLOGICAL REVIEWS, 1998, V165 (OCT), P181-194
ISSN: 0105-2896 Publication date: 19981000
Publisher: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK
Language: English Document Type: REVIEW (ABSTRACT AVAILABLE)

...Abstract: have used a novel approach which involves the ligation of

surface receptors on immature thymocytes with genetically engineered F(ab')₂ reagents, which, unlike conventional **antibodies**, do not aggregate the CD3 complex to such an extent as to induce extensive deletion of these cells. The experimental data presented in this **review** indicate that differentiation of the two mature CD4 and CD8 lineages occurs in response to distinct **intracellular** signals induced by particular receptor engagements. The data suggest that the tyrosine kinase p56(lck) (lck) plays a crucial role in determining lineage choice, in...

...deficient for a regulator of lck activity, CD45. A model of thymocyte differentiation is presented in which we propose that the relative balance of signals **delivered** by TCR engagement and lck activation determines lineage choice.

4/3,K/21 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.

05435647 Genuine Article#: VY582 No. References: 145
Title: GENE-THERAPY FOR CANCER THERAPEUTICS
Author(s): BILBAO G; CURIEL DT
Corporate Source: UNIV ALABAMA, GENE THERAPY PROGRAM, 824 6TH AVE S, WTI
620/BIRMINGHAM//AL/35294; UNIV ALABAMA, GENE THERAPY
PROGRAM/BIRMINGHAM//AL/35294; UNIV ALABAMA, CTR COMPREHENS
CANC/BIRMINGHAM//AL/35294
Journal: EXPERT OPINION ON THERAPEUTIC PATENTS, 1996, V6, N12 (DEC), P
1267-1284
ISSN: 1354-3776
Language: ENGLISH Document Type: REVIEW (Abstract Available)

Abstract: This **review** highlights current strategies and significant developments being employed in gene therapy for neoplastic diseases. Three main approaches, mutation compensation, molecular chemotherapy and genetic immunopotentialization, have been undertaken. Mutation compensation relies on strategies to ablate activated oncogenes at the level of DNA (triplexer), messenger RNA (antisense or ribozyme) or protein (**intracellular** single chain **antibodies**), and augment tumour suppressor gene expression. Molecular chemotherapy uses the *****delivery***** of a toxin gene to tumour cells for eradication. This can be accomplished by either transductional targeting, whereby the toxin is specifically **delivered** to the tumour, or by transcriptional targeting, whereby tumour-specific transcriptional activators are employed selectively to 'turn on' the toxin gene exclusively within the tumour...

4/3,K/22 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2005 Inst for Sci Info. All rts. reserv.

01961517 Genuine Article#: JQ020 No. References: 47
Title: IMMUNE-MECHANISMS OF ATHEROSCLEROSIS IN DIABETES-MELLITUS
Author(s): LOPESVIRELLA MF; VIRELLA G
Corporate Source: MED UNIV S CAROLINA, DEPT MED, DIV ENDOCRINOL METAB &
NUTR, 171 ASHLEY AVE/CHARLESTON//SC/29425; RALPH H JOHNSON DEPT VET
AFFAIRS MED CTR/CHARLESTON//SC/00000; MED UNIV S CAROLINA, DEPT
MICROBIOL & IMMUNOL/CHARLESTON//SC/29425
Journal: DIABETES, 1992, V41, S2 (OCT), P86-91
ISSN: 0012-1797
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: into foam cells and, in some cases, to induce endothelial cell damage. In addition, modified lipoproteins trigger an immune response leading to the formation of **antibodies** and then to the formation of LDL-containing immune complexes. In this *****review*****, we summarize the evidence linking LDL glycation and oxidation with **intracellular** accumulation of cholesterol esters and foam-cell formation, and we discuss their potential for inducing an autoimmune response and the formation of lipoprotein-containing immune...

...of LDL-ICs seems particularly significant, because these ICs are avidly taken up by macrophages through their F(c) receptors and induce not only massive **intracellular** accumulation of CE but also a paradoxical increase in LDL-receptor expression. Our experimental data suggest that the uptake of LDL-IC is facilitated by RBC adsorption, in agreement with the role of RBC in the adsorption of circulating IC and their *****delivery***** to phagocytic cells. In addition, macrophages are activated when ingesting LDL-IC and release IL-1beta and TNF-alpha which can contribute to the initiation...

4/3,K/23 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

02569581 2004044097
Antibody regulation of T-cell immunity: Implications for vaccine strategies against intracellular pathogens
Igietseme J.U.; Eko F.O.; He Q.; Black C.M.
ADDRESS: J.U. Igietseme, Molecular Pathogenesis Laboratory, Natl. Center for Infectious Disease, Mailstop C17, 1600 Clifton Road, Atlanta, GA 30333, United States
EMAIL: jigietseme@cdc.gov
Journal: Expert Review of Vaccines, 3/1 (23-34), 2004, United Kingdom
CODEN: ERVXA
ISSN: 1476-0584
DOCUMENT TYPE: Review
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 114

Intracellular microbial pathogens cause a plethora of diseases that pose a huge public health challenge. Efficacious prophylactic vaccines are needed to protect the population from this...

...of infectious diseases. Contemporary approaches to vaccine design are guided by the immunobiological paradigm that extracellular pathogens are controlled principally by humoral immunity, involving specific **antibodies**, whereas host protection against **intracellular** pathogens requires effectors of cell-mediated immunity. However, this distinct T-helper (Th) type 1 and 2 paradigm of host defense has encountered a major...

...to the reality that most antigens or vaccines induce mixed immune responses comprising of both humoral and CMI effectors. Besides, the true functional independence of **antibodies** and T-cells under in vivo physiologic conditions is uncertain. Recent findings have revealed that **antibodies** exert a significant immunoregulatory effect on T-cell immunity. Thus, a robust and protective T-cell memory response against microbial pathogens such as Chlamydia and Mycobacteria require an effective primary humoral immune response characterized by specific **antibody** isotypes whose role is to modulate Th1 activation via Fc receptors (FcR) by facilitating a rapid uptake, processing and presentation of pathogen-derived antigens for...

...defense wherein different components of the apparently disparate mixed immune responses elicited against a microbial pathogen function concertedly to maximize the principal effector mechanism. This ***review*** focuses on the essential role of both arms of the immune system in controlling **intracellular** microbial pathogens, especially the regulatory role of FcR-mediated **antibody** function in optimizing the induction of a protective Th1 response. The immunobiological implications are discussed in the context of vaccine design, **delivery** and evaluation against **intracellular** microbial pathogens of bacteria, fungi and parasitic origin.

4/3,K/24 (Item 2 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

01502121 2000174914
Emerging antibody-based HER2 (ErbB-2/neu) therapeutics
Krauss W.C.; Park J.W.; Kirpotin D.B.; Hong K.; Benz C.C.
ADDRESS: Dr. C.C. Benz, Division of Hematology-Oncology, University of California, Department of Medicine, 505 Parnassus Ave., San Francisco, CA 94143-1270, United States
EMAIL: benz@itsa.ucsf.edu
Journal: Breast Disease, 11/- (113-124), 2000, United States
CODEN: BRDIE
ISSN: 0888-6008
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 65

Targeting HER2(ErbB-2/neu) overexpressing tumor cells to selectively **deliver** anticancer agents and thereby reduce host toxicity represents a rational and emerging strategy for the treatment of breast and other epithelial cancers. The extracellular domain of the HER2 receptor tyrosine kinase is readily accessible to systemically administered **antibody**-based therapeutics, including growth-inhibiting monoclonsals such as rhuMABHER2 (trastuzumab/Herceptin(C)) as well as anti-HER2 immunotoxins, **antibody**-dependent enzyme prodrug therapy (ADEPT), and immune cell recruiting bispecific ***antibodies***. In addition to summarizing recent advances in these **antibody**-based strategies, this **review** focuses on preclinical advances in the development of anti-HER2 immunoliposomes (ILs) as a platform technology for targeted drug ***delivery***. Extensive in vitro and in vivo testing including efficacy and tumor uptake studies in multiple human tumor xenograft models now provide conclusive evidence for the...

...ILs-dox approaches clinical testing in patients with advanced HER2 overexpressing breast cancer, future applications of this novel targeting strategy will also broaden to include **intracellular delivery** of other anticancer agents as well as therapeutic nucleic acids (oligonucleotides, genes).

4/3,K/25 (Item 3 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

01426288 2000099874
Vaccination in the neonatal period and early infancy
Siegrist C.-A.
ADDRESS: C.-A. Siegrist, Department of Pediatrics, WHO Collab. Ctr. Neonatal Vaccinol., University of Geneva, 1 Michel-Server, 1211 Geneva 4, Switzerland

EMAIL: Claire-Anne.Siegrist@medecine.unige.ch
Journal: International Reviews of Immunology, 19/2-3 (195-219), 2000,
United Kingdom
CODEN: IRIME
ISSN: 0883-0185
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 69

Immune maturation is responsible for a progressive increase in **antibody** responses that can be elicited during the first year of life, such that neonatal immunization may currently not be expected to induce strong *****antibody***** responses. In contrast, B and T cell priming can be induced very early in life, without interference of maternal immunity. Strong IL-5 and IL-...
...IFN-gamma release capacity by early life APC and T cells both in young mice and infants, could contribute to the severity of infections with *****intracellular***** pathogens in early life. It calls for evaluation of novel **delivery** systems, adjuvants and/or prime-boost immunization strategies capable to meet the challenge of both strong neonatal immunogenicity and acceptable reactogenicity. The extent to which early life murine immunization models may be useful for preclinical evaluation of infant responses is outlined in this *****review*****.

4/3,K/26 (Item 4 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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01019249 1998265335
Molecular requirements for lineage commitment in the thymus -
Antibody-mediated receptor engagements reveal a central role for lck in lineage decisions
Basson M.A.; Bommhardt U.; Mee P.J.; Tybulewicz V.L.J.; Zamoyska R.
ADDRESS: R. Zamoyska, Division of Molecular Immunology, National Institute Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, United Kingdom
EMAIL: r-zamoys@nimr.mrc.ac.uk
Journal: Immunological Reviews, 165/- (181-194), 1998, Denmark
CODEN: IMRED
ISSN: 0105-2896
DOCUMENT TYPE: Review
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 94

...used a novel approach which involves the ligation of surface receptors on immature thymocytes with genetically engineered F(ab')₂ reagents, which, unlike conventional **antibodies**, do not aggregate the CD3 complex to such an extent as to induce extensive deletion of these cells. The experimental data presented in this **review** indicate that differentiation of the two mature CD4 and CD8 lineages occurs in response to distinct **intracellular** signals induced by particular receptor engagements. The data suggest that the tyrosine kinase p56(lck) plays a crucial role in determining lineage choice, in...

...deficient for a regulator of lck activity, CD45. A model of thymocyte differentiation is presented in which we propose that the relative balance of signals **delivered** by TCR engagement and lck activation determines lineage choice.

4/3,K/27 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

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12949855 EMBASE No: 2005005500

Future directions of liposome- and immunoliposome-based cancer therapeutics

Park J.W.; Benz C.C.; Martin F.J.

Seminars in Oncology (SEMIN. ONCOL.) (United States) 2004, 31/SUPPL. 13 (196-205)

CODEN: SOLGA ISSN: 0093-7754

PUBLISHER ITEM IDENTIFIER: S0093775404003860

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 68

Nanoscale drug **delivery** systems including liposomes, polymers, and other nanoparticles provide potential solutions for improved cancer therapeutics. Of these drug *****delivery***** systems, liposome-based agents, particularly liposomal anthracyclines, have had the greatest impact in oncology to date. Current liposomal drugs evolved from a number of design

...

...of passive targeting to tumor tissue. Future liposome therapeutics are building on these validated designs as well as on pharmacologic insights into their mechanisms of *****delivery*****. For example, camptothecin analogues, anti-angiogenesis agents, and antisense oligonucleotides each represent rational candidates for **delivery** in highly stabilized and long-circulating liposomes. For such agents, pegylated liposome **delivery** offers improved chemical stability of encapsulated drug, enhanced accumulation in tumors, and prolonged drug exposure. True molecular targeting can be achieved using liposomes linked to ligands such as monoclonal **antibody** fragments directed against cancer-associated antigens. Immunoliposomes combine *****antibody*****-mediated tumor recognition with liposomal **delivery** and, when designed for target cell internalization, provide *****intracellular***** drug release. Recent advances in immunoliposome design include rapid selection of phage **antibody**-derived scFv for targeting, and methods for conjugation of ligands to existing US Food and Drug Administration-approved liposomal drugs such as pegylated liposomal doxorubicin...

...binds to and internalizes in HER2-overexpressing tumor cells. The modular organization of immunoliposome technology enables a combinatorial approach in which a repertoire of monoclonal **antibody** fragments can be used in conjunction with a series of liposomal drugs to yield a new generation of molecularly targeted agents. (c) 2004 Elsevier Inc...

MEDICAL DESCRIPTORS:

...food and drug administration; drug approval; bone marrow suppression
--side effect--si; gastrointestinal toxicity--side effect--si; ovary cancer
--drug therapy--dt; human; clinical trial; **review**; priority journal

4/3,K/28 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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12685220 EMBASE No: 2004280630

Endothelial endocytic pathways: Gates for vascular drug delivery

Muro S.; Koval M.; Muzykantov V.

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Current Vascular Pharmacology (CURR. VASC. PHARMACOL.) (Netherlands)

2004, 2/3 (281-299)

CODEN: CVPUA ISSN: 1570-1611

DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 301

Vascular endothelium plays strategic roles in many drug **delivery** paradigms, both as an important therapeutic target itself and as a barrier for reaching tissues beyond the vascular wall. Diverse means are being developed to improve vascular drug **delivery** including stealth liposomes and polymer carriers. Affinity carriers including **antibodies** or peptides that specifically bind to endothelial surface determinants, either constitutive or pathological, enhance targeting of drugs to endothelial cells (EC) in diverse vascular areas...
...these two are less characteristic of generic EC) and the recently described Cell Adhesion Molecule (CAM)-mediated endocytosis. The latter may be of interest for **intracellular** drug **delivery** to EC involved in inflammation or thrombosis. The metabolism and effects of internalized drugs largely depend on the routes of **intracellular** trafficking, which may lead to degrading lysosomal compartments or other organelles, recycling to the plasma membrane or transcytosis to the basal surface of endothelium. The latter route, characteristic of caveoli-mediated endocytosis, may serve for trans-endothelial drug *****delivery*****. Paracellular trafficking, which can be enhanced under pathological conditions or by auxiliary agents, represents an alternative for transcytosis. Endothelial surface determinants involved in endocytosis, mechanisms...

...pathways, as well as specific characteristics of EC in different vascular areas, are discussed in detail in the context of modern paradigms of vascular drug *****delivery*****. (c) 2004 Bentham Science Publishers Ltd.
MEDICAL DESCRIPTORS:

...endocytosis; phagocytosis; pinocytosis; intracellular transport; thrombosis--etiology--et; cell compartmentalization; cell organelle; cell membrane; transcytosis; vasodilatation; antiinflammatory activity; antioxidant activity; drug binding site; human; nonhuman; **review**

4/3,K/29 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

10971426 EMBASE No: 2001014998
The principles of treatment of chronic inflammatory bowel disease
BEHANDLINGSPRINCIPPER FOR DE KRONISKE INFLAMMATORISKE TARMSYGDOMME
Binder V.; Munkholm P.
V. Binder, Medicinsk-Gastroenterol. Afd. C, Amtssygehuset i Herlev,
DK-2730 Herlev Denmark
Ugeskrift for Laeger (UGESKR. LAEG.) (Denmark) 01 JAN 2001, 163/1
(16-21)
CODEN: UGLAA ISSN: 0041-5782
DOCUMENT TYPE: Journal ; Review
LANGUAGE: DANISH SUMMARY LANGUAGE: ENGLISH; DANISH
NUMBER OF REFERENCES: 39

...of these diseases are to induce remission of outbreaks and to prevent outbreaks during remission. Available pharmaceutical products are 5-aminosalicylic acid preparations, with different **delivery** profiles in the gastrointestinal tract, glucocorticoids, and other immunosuppressants, especially azathioprine. New immunomodulating agents, with a specific effect on **intracellular** processes in the inflammatory cascade are now being developed, and infliximab, a TNF-alpha **antibody**, is now an accepted agent for use in severe, treatment-resistant cases of fistulising Crohn's disease. When medical treatment fails, surgical treatment is an...

MEDICAL DESCRIPTORS:

...ep; ulcerative colitis--surgery--su; Crohn disease--drug therapy--dt;
Crohn disease--epidemiology--ep; Crohn disease--surgery--su; incidence;
remission; inflammation; ileostomy; ileitis--complication--co; **review**

4/3,K/30 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

10648069 EMBASE No: 2000113009

Chlamydia trachomatis genital infections and single-dose azithromycin
therapy

Black C.M.; Byrne G.; Carlin E.; Gruber F.; Johnson F.N.; Mardh P.A.;
McClarty G.; Marra F.; Nuovo J.; Ostergaard L.; Paavonen J.; Patton D.L.;
Quinn T.C.; Raulston J.E.; Robinson A.; Rosenn M.F.; Scholes D.;
Steingrimsson O.; Worm A.-M.; Wyrick P.B.

C.M. Black, Box 15, Carnforth LA6 1HW United Kingdom

Reviews in Contemporary Pharmacotherapy (REV. CONTEMP. PHARMACOTHER.) (
United Kingdom) 2000, 11/3-4 (139-256)

CODEN: RCPHF ISSN: 0954-8602

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 999

The recognized species of Chlamydia are all prokaryotic obligate
intracellular parasites. Chlamydia trachomatis has a developmental
cycle which is complex and dimorphic. The infective forms (elementary
bodies) attach to and enter columnar and pseudostratified columnar...

...makes possible the introduction of screening programmes for Chlamydia
trachomatis; the use of a single oral dose of 1 g azithromycin enables
treatment to be **delivered** quickly, and with a minimum of
noncompliance. The identification of relevant risk factors permits
screening and treatment to be targeted, and there has been a...

...in the incidence of new infections where screening and treatment
programmes have been put in place. Nonculture techniques for identifying
Chlamydia trachomatis include direct fluorescent **antibody** tests,
enzyme immunoassays, nucleic acid detection and amplification procedures
(polymerase and ligase chain reactions). A rapid, but nonspecific,
leukocyte esterase dipstick test is also available...

MEDICAL DESCRIPTORS:

...etiology--et; urethritis--etiology--et; uterine cervicitis--complication
--co; vertigo--side effect--si; human; major clinical study; clinical trial
; meta analysis; male; female; adolescent; adult; **review**

4/3,K/31 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE
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07842130 EMBASE No: 1999088004

Disease modifying treatments for multiple sclerosis: What is on the
horizon?

Weilbach F.X.; Gold R.

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Würzburg Germany

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CNS Drugs (CNS DRUGS) (New Zealand) 1999, 11/2 (133-157)

CODEN: CNDRE ISSN: 1172-7047

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 255

...MS who have high disease activity. Aside from the therapeutic approaches now already introduced into the clinical armamentarium, newer agents and treatment concepts include monoclonal **antibodies**, intravenous immunoglobulins, modulators of trimolecular complex and agents that interact with costimulatory molecules. Cytokine modulators and inhibitors of cell adhesion are promising candidates but their...

...MS. The clinical evaluation of new treatment approaches will be difficult given the heterogeneity and unpredictable course of the disorder. Interesting future therapeutic approaches include **intracellular** signal transduction modulators, vitamins and newer immunosuppressants. Gene therapy, vaccination with naked DNA or dendritic cells may also turn out to be useful. Besides developing new immunotherapies it seems indispensable to improve **delivery** of symptomatic treatment and rehabilitation aiming at the quality of life of individual MS patients. Identification of disease course predictors or treatment response will improve...

MEDICAL DESCRIPTORS:

...desensitization; immunostimulation; passive immunization; antimicrobial therapy; drug mechanism; drug efficacy; recurrent disease; drug research; cell adhesion; tissue repair; human; oral drug administration; intravenous drug administration; **review**; priority journal

4/3,K/32 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

07679377 EMBASE No: 1999163410

Heat shock protein-based therapeutic strategies against human immunodeficiency virus type I infection

Brenner B.G.; Wainberg M.A.

Dr. B.G. Brenner, Lady Davis Institute, Jewish General Hospital, 3755 Cote Ste. Catherine Road, Montreal, Que. Canada

AUTHOR EMAIL: mdbl@musica.mcgill.ca

Infectious Disease in Obstetrics and Gynecology (INFECT. DIS. OBSTET. GYNECOL.) (United States) 1999, 7/1-2 (80-90)

CODEN: IDOGE ISSN: 1064-7449

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 82

Heat shock proteins (hsps) and cyclophilins (CypA) are **intracellular** chaperone molecules that facilitate protein folding and assembly. These proteins are selectively expressed in cells following exposure to a range of stress stimuli, including viral infection. Hsp species are highly immunogenic, eliciting humoral, cytotoxic T lymphocyte (CTL), and natural killer (NK) cell responses against viruses, tumours, and infectious diseases. This *****review***** discusses the roles of stress proteins in immunity and viral life cycles, vis-a-vis the development of Hsp-based therapeutic strategies against human immunodeficiency...

...hsp70 during single-cycle HIV infections. These species redistribute to the cell surface following HIV-infection and heat stress, serving as targets for NK and *****antibody***** -dependent cellular cytotoxicity. Co-immunoprecipitation and Western blot studies show that hsp27, hsp70, and hsp78 complex with HIV-1 viral proteins *****intracellularly*****. Hsp70, hsp56, and CypA are assembled into HIV-1 virions. The ability of hsps to interact with HIV-1 viral proteins, combined with their inherent adjuvant and immunogenic properties, indicates that hsps may serve as vehicles for antigen **delivery** and the design of vaccines against acquired immunodeficiency syndrome.

4/3,K/33 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

07458668 EMBASE No: 1998376529
Gene therapy: Principles and perspectives
GENSKO LIJECENJE: NACELA, DOMETI I PERSPEKTIVE
Pavelic J.; Slade N.; Galetic I.; Pavelic K.
J. Pavelic, Zavod za Molekularnu Medicinu, Institut Ruder Boskovic,
Zagreb Croatia
Pharmaca (PHARMACA) (Croatia) 1998, 36/3 (151-170)
CODEN: PHAMB ISSN: 0031-6857
DOCUMENT TYPE: Journal; Review
LANGUAGE: SERBOCROATIAN SUMMARY LANGUAGE: ENGLISH; SERBOCROATIAN
NUMBER OF REFERENCES: 31

The development of methods for **delivering** genes to mammalian cells has provided the possibility of treating human cancers as well as other genetic disorders by gene-based therapies. Beside the introduction...

...therapy might be conducted so that the gene transcript as well as the final gene productprotein, are attacked by either antisense therapy, or ribozymes or *****intracellular***** monoclonal *****antibodies*****. More than 40 human gene transfers have been initiated since the introduction of this therapeutic approach in 1989. However, despite substantial progress, a number of key technical issues need to be resolved. They include efficient **delivery** of genes into appropriate target cells transduced with the therapeutic gene, sustained expression of the transgene in human tissues, and immunogenicity of the transduced cells...

MEDICAL DESCRIPTORS:

gene targeting; gene transfer; gene expression; immunogenicity;
immunotherapy; virus vector; virus recombinant; **review**

4/3,K/34 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

06383923 EMBASE No: 1996049605
New approaches to mucosal immunization
Langermann S.
Mucosal Immunity and Vaccines, MedImmune Inc., 35 West Watkins Mill
Road, Gaithersburg, MD 20878 United States
Seminars in Gastrointestinal Disease (SEMIN. GASTROINTEST. DIS.) (United States) 1996, 7/1 (12-18)
CODEN: SGDIE ISSN: 1049-5118
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

An ideal vaccine ought to produce long-term protective immune responses against a pathogen. These responses include humoral *****antibodies*****, which neutralize invasive microorganisms, and cytotoxic T cells, which destroy *****intracellular***** pathogens. Both types of responses can be induced by parenteral immunization, which is how most vaccines have been administered to date. Given that most bacteria and viruses initiate infections at mucosal surfaces where secretory immunoglobulin A (slgA) **antibodies** are thought to play an important role in prevention of microbial attachment and colonization, there may be an added advantage for vaccines that stimulate long-lasting secretory immunity against pathogens as well. A prerequisite for the generation of slgA **antibodies** is that antigens be *****delivered***** at mucosal sites. This *****review***** focuses on novel

mucosal vaccination strategies aimed at inducing such secretory immunity to pathogens, while at the same time, stimulating humoral and, in some cases

MEDICAL DESCRIPTORS:

bacterial colonization; bacterium adherence; cytotoxic t lymphocyte; immune response; immunization; nonhuman; **review**

4/3,K/35 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

05698422 EMBASE No: 1994112472
Quo vadis: Perinatal AIDS issues - 2004
Weiss S.H.; Louria D.B.
Infectious Diseases Epidemiol. Div., Preventive Med./Commun. Health
Dept., UMDNJ-New Jersey Medical School, 30 Bergen Street, Newark, NJ 07107
United States
Clinics in Perinatology (CLIN. PERINATOL.) (United States) 1994, 21/1
(179-198)
CODEN: CLPED ISSN: 0095-5108
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

...to the fetus in some cases. On the other hand, some small uncontrolled studies have not demonstrated a reduction in HIV infection rates among children **delivered** by caesarian **delivery**, and examination of some aborted fetuses indicate HIV transmission can occur by the first trimester. However, this may reflect selection phenomena for more complicated pregnancies...

...as late as labor might become effective as prevention strategies in terms of perinatal transmission. In addition to antiretroviral therapy, trials of purified anti-HIV **antibodies** derived from the plasma of HIV-infected persons (HIVIG) have been planned. These have been delayed, in part, by vendor liability concerns. Although HIVIG cannot eliminate **intracellular** HIV infection, such **antibodies** may reduce the level of free virus in the peripheral blood. Vaccination strategies that boost cellular immunity, either in the mother before **delivery** or in the neonate, may also be useful in prevention. Many women at highest risk of HIV receive little or no prenatal care. Thus, a...

MEDICAL DESCRIPTORS:

disease control; epidemic; futurology; health care planning; health service ; human; priority journal; **review**; society; world health organization

4/3,K/36 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2005 Elsevier Science B.V. All rts. reserv.

03360674 EMBASE No: 1987113251
Live oral Salmonella vaccines: Potential use of attenuated strains as carriers of heterologous antigens to the immune system
Dogan G.; Hormaeche C.E.; Maskell D.J.
Wellcome Research Laboratories, Beckenham, Kent BR3 3BS United Kingdom
Parasite Immunology (PARASITE IMMUNOL.) (United Kingdom) 1987, 9/2
(151-160)
CODEN: PAIMD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

...vaccine. Mice infected orally with a Salmonella typhimurium aroA vaccine expressing the Escherichia coli heat-labile toxin B subunit

developed both a secretory and serum **antibody** response to this antigen. These serum *****antibodies***** were able to neutralise the activity of E. coli heat-labile toxin in tissue culture assays. A humoral and cell-mediated (DTH) immune response was detected against beta galactosidase, an **intracellular** antigen, in mice infected with an aroA vaccine expressing this cloned antigen. The prospects for the development of live Salmonella vaccines as a method for **delivering** heterologous antigens derived from bacteria, viruses and parasites is discussed.

MEDICAL DESCRIPTORS:

mouse; priority journal; oral drug administration; **review**; human; normal human; prevention

4/3,K/37 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus
(c)2005 Japan Science and Tech Corp(JST). All rts. reserv.

05244798 JICST ACCESSION NUMBER: 02A0678171 FILE SEGMENT: JICST-E
Liposomes for tumor-targeted therapy.

ITO AKIRA (1); HONDA HIROYUKI (1); KOBAYASHI TAKESHI (1)

(1) Nagoya Univ., Graduate School of Engineering, JPN

Drug Deliv Syst, 2002, VOL.17,NO.4, PAGE.347-354, FIG.6, REF.16

JOURNAL NUMBER: X0225AAO ISSN NO: 0913-5006 CODEN: DDSYE

UNIVERSAL DECIMAL CLASSIFICATION: 615.45.033 616-006-08-092.4

LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal

ARTICLE TYPE: Review article

MEDIA TYPE: Printed Publication

...ABSTRACT: Liposomalization of various drugs has revealed the enhancement of their efficacy: Since liposomes can reduce the side effect of the drugs by the site-specific **delivery**, **intracellular** targeting, and controlled release of drugs, many functional liposomes have been developed including cationic liposomes and **antibody**-conjugating immunoliposomes. In this article, the preparation and characterization of functional liposomes are discussed. We have developed **intracellular** hyperthermia using magnetic nanoparticles (magnetites) by the feature that magnetites can generate heat under high frequency alternative magnetic field. In addition, magnetites affect the magnetic...

...contrast enhancement reagent for MRI. Therefore, if magnetite can be accumulated only in tumor tissue, they can afford cancer diagnosis and tumor-specific hyperthermia. To *****deliver***** the magnetites toward tumors, two kinds of functional liposomes have been developed, which were "magnetite cationic liposomes (MCLs)" and "Fab'-conjugating magnetoliposomes (FMLs)". MCLs were...

...the high affinity to the tumor cells. On the other hands, FMLs were designed for "missile liposomes" which can accumulate in the tumor by antigens-**antibody** reaction even in the case of intravascular injection. Here, we *****review***** these functional liposomes and discussed how to achieve the ultimate goal for tumor targeting. (author abst.)

4/3,K/38 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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04755405 H.W. WILSON RECORD NUMBER: BGSA02005405 (USE FORMAT 7 FOR FULLTEXT)

Trafficking of canalicular ABC transporters in hepatocytes.

Kipp, Helmut

Arias, Irwin M

Annual Review of Physiology v. 64 (2002) p. 595-608

SPECIAL FEATURES: bibl il ISSN: 0066-4278

LANGUAGE: English

COUNTRY OF PUBLICATION: United States

WORD COUNT: 5602

(USE FORMAT 7 FOR FULLTEXT)

TEXT:

... ABC transporters to the canalicular membrane. Therefore, intracellular traffic and regulation of canalicular ABC transporters are critical for bile formation under physiological conditions (13). This **review** summarizes recent knowledge regarding intrahepatic distribution, regulation, and traffic of canalicular ABC transporters.

TRAFFIC OF NEWLY SYNTHESIZED ABC TRANSPORTERS IN HEPATOCYTES

Membrane targeting of the...

...min, 1 h, 2 h, and 3 h in purified canalicular membrane vesicles (CMV), SMV, and Golgi membranes from rat liver by immunoprecipitation with specific *****antibodies*****. These studies (18) confirmed the transcytotic pathway for apical targeting of newly synthesized cCAM105 (HA4), as described above (14). In contrast, at no time between...

...SPGP were not initially transferred to the basolateral membrane, i.e., their post-Golgi trafficking differed. After passage through Golgi, MDR1 and MDR2 were rapidly **delivered** directly to the bile canaliculus, whereas Golgi-to-bile canaliculus trafficking of SPGP involved additional intermediate steps. At 1 h after metabolic labeling, only the...

...therefore, had not reached the cell surface, which occurred 2 h after metabolic labeling. The most likely explanation is that SPGP is sequestered in an **intracellular** pool prior to **delivery** to the canalicular membrane. Intrahepatic sequestering of newly synthesized SPGP was demonstrated in a later study, which included a combined endosomal fraction in metabolic labeling...

4/3,K/39 (Item 2 from file: 98)

DIALOG(R)File 98:General Sci Abs/Full-Text

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04274000 H.W. WILSON RECORD NUMBER: BGSA00024000 (USE FORMAT 7 FOR FULLTEXT)

Legionella pneumophila pathogenesis: a fateful journey from amoebae to macrophages.

Swanson, M. S

Hammer, B. K

Annual Review of Microbiology v. 54 (2000) p. 567-613

SPECIAL FEATURES: bibl diag tab ISSN: 0066-4227

LANGUAGE: English

COUNTRY OF PUBLICATION: United States

WORD COUNT: 21515

(USE FORMAT 7 FOR FULLTEXT)

TEXT:

... to the legionellae, they are rarely associated with disease (191). Consequently, laboratory studies of Legionella pathogenesis have focused primarily on L. pneumophila, as does this *****review*****. A comprehensive

description of the genus Legionella is provided by Benson & Fields (22).

AN AIRBORNE RESPIRATORY PATHOGEN

People most often become infected with *L. pneumophila*...response paradigm provides a conceptual framework for the extensive phenotypic variation that has been documented for *L. pneumophila* cultured under different conditions (Figure 1).

THE INTRACELLULAR PATHWAY

THE NASCENT PHAGOSOME

COILING PHAGOSOMES

Macrophages and amoebae engulf *L. pneumophila* within coils of plasma membrane (27, 124). However, this unusual mode of entry does not appear to be necessary or sufficient for ***intracellular*** survival of *L. pneumophila* in professional phagocytes. Heat-killed, fixed, and avirulent *L. pneumophila* are also ingested within coiled phagosomes, but these particles are ***delivered*** to the endosomal compartment (27, 123, 125). Conversely, *L. pneumophila* that have been opsonized with specific ***antibody*** form conventional phagosomes, but evade lysosomes (124). In addition, although *L. pneumophila* replicate in *H. vermiformis*, coiling phagosomes have not been detected in these cells...

4/3,K/40 (Item 3 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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03805295 H.W. WILSON RECORD NUMBER: BGSA98055295 (USE FORMAT 7 FOR FULLTEXT)

The HIV-1 Rev protein.

Pollard, Victoria W

Malim, Michael H

Annual Review of Microbiology v. 52 (1998) p. 491-532

SPECIAL FEATURES: bibl il ISSN: 0066-4227

LANGUAGE: English

COUNTRY OF PUBLICATION: United States

WORD COUNT: 20110

(USE FORMAT 7 FOR FULLTEXT)

...ABSTRACT: export. HIV-1 Rev therefore represents an excellent system with which to study aspects of transport across the nuclear envelope. With permission, from the Annual **Review** of Microbiology, Volume 52, 1998, by Annual Reviews Inc. (<http://www.annurev.org>)....

TEXT:

... of the preferred model systems with which one can study the signal-mediated export of macromolecules from the nucleus to the cytoplasm. For simplicity, this **review** is organized chronologically, starting with the discovery of Rev in 1986, proceeding through its assignment as a trans-activator of RNA nuclear export, and culminating...to the cytoplasm. The first to be discovered is typified by the Rev trans-activator of HIV-1 and is the major subject of this ***review***. Here, a virally encoded protein, Rev, interacts directly with a cis-acting target, the Rev response element (RRE), which is present in all incompletely spliced...structural gene expression in cultured cells (233, 234). Related small-molecule inhibitors may therefore represent good candidates for further development.

At various points during this **review**, inactive mutant proteins that exhibit dominant negative (trans-dominant) phenotypes with respect to their wild-type counterparts have been described. In the case of Rev...

...sink" for Rev within cells such that Rev is diverted away from its

RRE-containing RNA targets. In one example, Rev-specific single-chain variable **antibody** fragments (SFvs) have been used to sequester Rev in the cytoplasm (43, 44). In the other, multiple stable copies of the RRE are expressed in...

...these RNAs have been termed RNA decoys. Importantly, and as with all genetic-based therapies, the major challenge with each of these four versions of "intracellular immunization" is to **deliver** the inhibitory sequences to the critical cell targets with sufficient simplicity and effectiveness (110).

Added material

Victoria W. Pollard

Department of Microbiology, University of Pennsylvania...

4/3,K/41 (Item 4 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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03546277 H.W. WILSON RECORD NUMBER: BGS197046277 (USE FORMAT 7 FOR FULLTEXT)

Interaction of antigens and antibodies at mucosal surfaces.

Lamm, Michael E

Annual Review of Microbiology (Annu Rev Microbiol) v. 51 ('97) p. 311-40

SPECIAL FEATURES: bibl il ISSN: 0066-4227

LANGUAGE: English

COUNTRY OF PUBLICATION: United States

WORD COUNT: 13855

(USE FORMAT 7 FOR FULLTEXT)

ABSTRACT: Infections often involve the mucosal surfaces of the body, which form a boundary with the outside world. This *****review***** focuses on immunoglobulin A (IgA) antibodies because IgA is the principal mucosal antibody class. IgA is synthesized by local plasma cells and has a specific ...

TEXT:

... of mucosal defense against microbes are both cellular (mediated by T lymphocytes) and humoral (mediated by antibodies), with the latter as the subject of this *****review*****. First, some features of the antimicrobial actions of antibodies in general will be mentioned briefly. For example, specific antibodies can bind to microbes and to...

...mediated mechanism for selectively transporting IgA across the epithelial cells that line mucous membranes.

Because IgA is so dominant in mucosal tissues and secretions, this **review** will emphasize the interactions between IgA antibodies and antigens and their significance for host defense against ...antibodies against internal viral proteins are much less effective (MB Mazanec, personal communication).

Recent data in animal model systems have provided in vivo evidence for *****intracellular***** virus neutralization by IgA *****antibody*****. IgA monoclonal **antibodies** to outer and inner capsid proteins of rotavirus were **delivered** systemically and evaluated for their ability to prevent or cure enteritis in mice (13). IgA *****antibodies***** to the inner capsid protein VP6 were highly effective, in both respects, whereas IgA *****antibodies***** to the outer capsid protein VP4 were ineffective. These in vivo results were opposite to those obtained in an in vitro neutralization assay, in which **antibodies** to the external capsid protein were neutralizing and *****antibodies***** to the inner capsid protein were not. The results for the in vitro neutralization assay are to be expected because **antibodies** to proteins displayed on the surface of the virus

(such as VP4) can combine with intact virus, whereas **antibodies** to proteins that are not on the surface (such as VP6) cannot. The observation that IgA **antibodies** that were incapable of neutralizing virus in a plaque reduction assay (or when presented to the luminal aspect of the intestinal mucosa in vivo) were...that use mucous membranes as portals of entry. Although an in-depth consideration of current approaches to mucosal immunization is beyond the scope of this **review**, some general considerations and examples are mentioned.

The origin and differentiation of the mucosal plasma cells that secrete IgA are relevant to the specificity of...

4/3,K/42 (Item 5 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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03546274 H.W. WILSON RECORD NUMBER: BGS197046274 (USE FORMAT 7 FOR FULLTEXT)

Intracellular antibodies (intrabodies) for gene therapy of infectious diseases.

Rondon, Isaac J
Marasco, Wayne A

Annual Review of Microbiology (Annu Rev Microbiol) v. 51 ('97) p. 257-83

SPECIAL FEATURES: bibl il ISSN: 0066-4227

LANGUAGE: English

COUNTRY OF PUBLICATION: United States

WORD COUNT: 11098

(USE FORMAT 7 FOR FULLTEXT)

...ABSTRACT: as targets. These intrabodies have demonstrated their versatility by controlling early as well as late events of the viral life cycle. In this article, we *****review***** studies of the use of intrabodies as research tools and therapeutic agents against HIV-1. Reprinted by permission of the publisher.

TEXT:

... have been investigated to control the progress of this virus to infectious disease. Among these strategies are immune reconstitution, nucleic acid-based therapeutic vaccines, and **intracellular** immunization. Immune reconstitution or adoptive cell therapy for HIV-1 infection involves ex vivo expansion of selected, and sometimes genetically modified, T cell populations (e...

...cytotoxic T lymphocytes (CTL) and CD4 lymphocytes), followed by their reinfusion into the HIV-1-infected patient (125). Nucleic acid-based therapeutic vaccines involve direct *****delivery***** of HIV-1 genes (e.g. env) to mimic viral infection; the expression of viral proteins encoded by these nucleic acids elicits both cellular and humoral responses (149). Lastly, **intracellular** immunization transfers a therapeutic gene into target cells to render them resistant to viral replication. The resistant cells will then limit the spread of the virus in the patient (3). Different modalities of **intracellular** immunization have been developed, broadly divided into two categories: RNA-based and protein-based suppressors. The RNA-based suppressors include antisense RNA, ribozymes (130), and...

...virus replication. The RNA-based suppressors are limited to the cytoplasmic compartment. The protein-based suppressors include transdominant mutant proteins (91), suicide molecules (14), and *****intracellular***** *****antibodies***** (96). Transdominant mutant proteins are altered viral proteins that compete with the native viral protein. Suicide molecules, unlike other approaches, do not protect the cells but

rather destroy the infected cell. ***Intracellular*** ***antibodies*** , hereafter referred to as "intrabodies," are the focus of this ***review*** . Intrabodies are synthesized by the cell and directed to a particular cellular compartment to inactivate, in a highly specific manner, a target molecule.

Early studies...

...field of gene transfer (137) with intrabody technology holds great promise in the future for genetically treating a number of infections and other diseases.

This **review** concentrates on the expression of intrabodies against HIV-1 proteins with relevance to future applications in gene therapy. It does not include intrabodies against the...because of the failures of many single agents to halt the spread of HIV-1 (83).

In the case of intrabodies, studies presented in this **review** demonstrate that a variety of HIV-1 proteins are sensitive to neutralization by intrabodies and inhibit HIV-1 replication. This HIV-1 inhibition by intrabodies...antibodies from phage display repertoires to a single epitope of an antigen. Bio/Technology 12:899-903

68. Jiang W, Venugopal K, Gould EA. 1995. ***Intracellular*** interference of tickborne flavivirus infection by using a single-chain ***antibody*** fragment ***delivered*** by recombinant sindbis virus. J. Virol. 69:1044-49

69. Johnson MS, McClure MA, Feng D-F, Gray J, Doolittle RF. 1986. Computer analysis of...

4/3,K/43 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0313584 DBR Accession No.: 2003-14724

Immunological hurdles to lung gene therapy - plasmid, liposome, adeno virus or adeno-associated virus vector-mediated gene transfer for cystic fibrosis, alpha-1-antitrypsin deficiency or lung cancer gene therapy; a **review**

AUTHOR: FERRARI S; GRIESENBACH U; GEDDES DM; ALTON E

CORPORATE AFFILIATE: Imperial Coll Fac Med

CORPORATE SOURCE: Ferrari S, Imperial Coll Fac Med, Natl Heart and Lung Inst, Dept Gene Therapy, UK Fibrosis Gene Therapy Consortium, London SW3 6LR, England

JOURNAL: CLINICAL AND EXPERIMENTAL IMMUNOLOGY (132, 1, 1-8) 2003

ISSN: 0009-9104

LANGUAGE: English

...plasmid, liposome, adeno virus or adeno-associated virus vector-mediated gene transfer for cystic fibrosis, alpha-1-antitrypsin deficiency or lung cancer gene therapy; a **review**

ABSTRACT: AUTHOR ABSTRACT - Gene **delivery** has the potential to offer effective treatment to patients with life-threatening lung diseases such as cystic fibrosis, alpha(1)-antitrypsin deficiency and lung cancer...

... trials have shown that, in principle, gene transfer to the lung is feasible and safe. However, gene expression from both viral and non-viral gene ***delivery*** systems has been inefficient. In addition to extra- and **intracellular** barriers, the host innate and acquired immune system represents a major barrier to successful gene transfer to the lung. Results from studies in experimental animals and clinical trials have shown that inflammatory, **antibody** and T cell responses can limit transgene expression duration and readministration of the gene transfer vector. We will ***review*** here how the development of pharmacological and/or immunological agents can modulate

the host immune system and the limitations of these strategies. A better understanding...

DESCRIPTORS: ...mediated gene transfer, expression in patient lung, animal host cell, immune response, appl. cystic fibrosis, alpha-1-antitrypsin deficiency, lung cancer gene therapy, clinical trial, **review** lipofection transfection parvo virus 7q31.2 chromosome-7 tumor (22, 24)

4/3,K/44 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0254203 DBR Accession Number: 2000-08693
Gene therapy: from bench to bedside: Lenti virus vectors for gene therapy
- e.g. HIV virus-1 and HIV virus-2 retro virus vectors and their packaging cell cultures; a **review**
AUTHOR: Lever A M L; Kaye J F; McCann E; Chadwick D; Dorman N; Thomas J; Zhao J
CORPORATE AFFILIATE: Univ.Cambridge
CORPORATE SOURCE: University of Cambridge, Department of Medicine, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ, UK.
JOURNAL: Biochem.Soc.Trans. (27, Pt.6, 841-47) 1999
ISSN: 0300-5127 CODEN: BCSTB5
LANGUAGE: English

- e.g. HIV virus-1 and HIV virus-2 retro virus vectors and their packaging cell cultures; a **review**

...ABSTRACT: versus translation; lenti virus vector retro virus vector systems; lenti virus vector design; lenti virus packaging cell cultures; transient co-transfection and vector production; genes **delivered** by lenti virus vectors (mainly marker genes, but a few potential therapeutics such as anti HIV virus ribozymes, decoy RNAs, thymidine-kinase, cystic fibrosis transmembrane regulatory protein, interleukin-4, **intracellular antibodies**); other lenti virus-based vectors (chimeric HIV virus-1 helper packaging an HIV2 vector, FIV virus vector, goat arthritis-encephalitis virus vector and horse-infectious...

DESCRIPTORS: lenti virus vector, HIV virus-1 vector, HIV virus-2 vector, design, packaging cell culture, packaging signal, transient co-transfection, appl. gene therapy, *****review***** retro virus leuko virus gene transfer (Vol.19, No.15)

4/3,K/45 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0239844 DBR Accession No.: 1999-09945
A role for intracellular immunization in chemosensitization of tumor cells?
- nucleic acid vaccine, ribozyme and antisense molecules for use in cancer gene therapy; a **review**
AUTHOR: Piche A; Rancourt C
CORPORATE AFFILIATE: Univ.Sherbrooke
CORPORATE SOURCE: Departement de Microbiologie, Faculte de Medecine, Universite de Sherbrooke, 3001 12ieme Avenue Nord, Sherbrooke, Quebec J1H 5N4, Canada.
JOURNAL: Gene Ther. (6, 7, 1202-09) 1999
ISSN: 0969-7128 CODEN: GETHEC
LANGUAGE: English

- nucleic acid vaccine, ribozyme and antisense molecules for use in cancer gene therapy; a **review**

...ABSTRACT: or that relapse after initial response to chemotherapy is a

major clinical challenge due to acquired drug resistance and cross-resistance. The potential applications of ***intracellular*** immunization to modulate the resistance phenotype of tumor cells are reviewed. Topics discussed include: ***intracellular*** **antibodies**, including erbB-2, EGF-receptor, anti-apoptotic proteins, Ras proteins, P-glycoprotein and cyclin-D1; antisense oligonucleotides, including erbB-2, EGF-receptor, cyclin-D1, Bcl-2 and other antisense nucleic acid molecules; and ribozymes, including MDR-1 and Bcl-2. In conclusion, ***intracellular*** use of nucleic acid vaccines can be used to overcome drug resistance, in conjunction with chemotherapy in cancer treatment. The choice of gene ***delivery*** system depends on the nature of the strategy and the context of the target tissue. (119 ref)

DESCRIPTORS: nucleic acid vaccine, ribozyme, antisense molecule, tumor cell chemosensitization, appl. cancer gene therapy, ***review*** RNA enzyme gene transfer (Vol.18, No.7)

4/3,K/46 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0180900 DBR Accession No.: 95-08920
Genetic delivery of enzymes for cancer therapy - use for prodrug activation as a means of gene therapy; a **review**
AUTHOR: Deonarain M P; Spooner R A; Epenetos A A
CORPORATE AFFILIATE: Imperial-Cancer-Res.Fund Hammersmith-Hosp.London
CORPORATE SOURCE: Tumor Targeting Laboratory, ICRF Oncology Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS, UK.
JOURNAL: Gene Ther. (2, 4, 235-44) 1995
ISSN: 0969-7128 CODEN: 4352W
LANGUAGE: English

- use for prodrug activation as a means of gene therapy; a **review**
...ABSTRACT: of tumor-specific promoters, some of which may be exploited for tumor-specific enzyme expression. The gene expression of prodrug activating enzymes rather than their **antibody-mediated delivery** for cancer therapy may overcome some of the problems associated with the latter approach. Gene ***delivery*** is usually achieved by a retro virus or by a physical process (naked DNA injection). The enzyme is expressed ***intracellularly***, so that drug activation occurs inside the cell. There are only 2 established systems for gene-mediated enzyme expression for prodrug activation. These are thymidine-kinase (EC-2.7.1.21) and cytosine-deaminase (EC-3.5.4.1). However, many others are under development. ***Delivery*** of suicide enzymes is also envisaged. More research is needed to enable full exploitation of the transcriptional differences between tumor and normal cells so that...

DESCRIPTORS: gene-mediated enzyme expression for prodrug activation, cancer gene therapy, ***review*** tumor (Vol.14, No.15)

4/3,K/47 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0176510 DBR Accession No.: 95-03331
Gene therapy and immune restoration for HIV disease - including intracellular immunization and genetic immunization; a **review**
AUTHOR: Bridges S H; +Sarver N
CORPORATE AFFILIATE: Nat.Inst.Allergy+Infec.Dis.Bethesda
CORPORATE SOURCE: Targeted Interventions Branch, Division of AIDS, National

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Maryland 20892-7620, USA.

JOURNAL: Lancet (345, 8947, 427-32) 1995

ISSN: 0140-6736 CODEN: LANCAO

LANGUAGE: English

- including intracellular immunization and genetic immunization; a

review

...ABSTRACT: study reviews strategies that can target the viral, immunological and cellular components of HIV virus disease, e.g. gene therapy, immune reconstitution, genetic immunization and ***intracellular*** immunization. Gene therapy strategies include RNA-based suppressors. RNA decoys compete with viral RNAs for binding essential HIV virus regulatory proteins. Ribozymes inactivate HIV virus

...

... at specific sequences. Transdominant mutant proteins can compete with the wild-type protein to suppress virus functions, e.g. mutant Rev protein. HIV virus-specific ***intracellular*** single chain **antibodies** sequester viral proteins in appropriate cellular compartments. ***Intracellular*** expression of suicide molecules may be used to eradicate HIV virus-infected cells. Gene ***delivery*** mechanisms have included mouse retro virus vectors, adeno-associated virus vectors, non-pathogenic HIV virus vectors, and lipofection to ***deliver*** genes to target cells. Adoptive immunotherapy has focused on the expansion of CD8 and CD4 lymphocytes, with their reinfusion into infected patients. Genetic immunization may...

DESCRIPTORS: HIV virus infection gene therapy, intracellular immunization, genetic immunization, **review** leuko virus retro virus gene transfer RNA decoy ribozyme single chain antibody adeno virus adeno-associated virus parvo virus lipofection liposome transfection adoptive immunotherapy AIDS...

4/3,K/48 (Item 1 from file: 370)

DIALOG(R)File 370:Science

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00504955 (USE 9 FOR FULLTEXT)

Unconventional Myosins in Cell Movement, Membrane Traffic, and Signal Transduction

Mermall, Valerie; Post, Penny L.; Mooseker, Mark S.

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Science Vol. 279 5350 pp. 527

Publication Date: 1-23-1998 (980123) Publication Year: 1998

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Articles

Word Count: 4435

(THIS IS THE FULLTEXT)

...Text: has been documented (B4) , suggesting that there may be a wide range of functions for actin-based motors in the cell (Table 1). In this **review** we focus on recent evidence for functions associated with the so-called "unconventional" nonmuscle myosins (Table 1). The reader is referred to comprehensive reviews for...

...the male germ unit along pollen tubes (B7) . Although several plant myosin genes have been cloned, the specific myosins involved in these phenomena remain unidentified. ***Antibodies*** raised against heterologous myosins react with small particles and organelles in Lilium longiflorum pollen tubes; these antigens may participate in transport through the pollen tube...

...sequence motif in the tail region (Figs. 1 and 2). 95F myosin-associated particles undergo cell cycle-dependent, 95F myosin-dependent directed movement in vivo. ***Antibody*** inhibition of 95F myosin blocks the directed transport of these particles and results in misorganization of the cortical actin cytoskeleton (B10). In mice with mutations...SER does not extend into the dendrites of Purkinje cells of dilute mice (B18) and a presumed dilute rat (B20); this may disrupt regulation of ***intracellular*** Ca.sup(2+) and result in the seizures observed in these animals (Fig. 3...

...partially colocalizes with melanosomes and ER (B23) (B24). Although the function of M5 in melanosome distribution remains undetermined, data suggest roles for M5 in melanosome **delivery** to dendrites, tethering of melanosomes in dendritic arbors (B23) (B24), or both (Fig. 3...
...dilute mice, patients with Griscelli disease have partial albinism and a range of neurological defects; in addition, they exhibit immunological defects including hypogammaglobulinemia and deficient **antibody** production (B26...Figure Removed

Begin Table : Columns 1 - 3 of 3

Caption:

Potential functions for unconventional myosins discussed in this
review

Potential function	Myosin	Class
Cell growth and development	Dictyostelium myoA, B, C	I
	Yeast Myo3p, 5p	I
	Aspergillus MYOA	I
Cell movement	Dictyostelium myoA, B...	

References and Notes:

...of M1 have been identified in addition to the subclass first characterized in Acanthamoeba and Dictyostelium. Dictyostelium have at least six M1 isoforms. For a ***review*** of M1s, see (B43...

4/3,K/49 (Item 2 from file: 370)
DIALOG(R)File 370:Science
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00504186 (USE 9 FOR FULLTEXT)
Interleukin-3-Induced Phosphorylation of BAD Through the Protein Kinase Akt

Peso, Luis del; Gonzalez-Garcia, Maribel; Page, Carmen; Herrera, Roman; Nunez, Gabriel
L. del Peso, M. Gonzalez-Garcia, C. Page, G. Nunez, Department of Pathology and Comprehensive Cancer Center, University of Michigan Medical School, Ann Arbor, MI 48109, USA.; R. Herrera, Department of Signal Transduction, Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, Ann Arbor, MI 48105, USA.
Science Vol. 278 5338 pp. 687
Publication Date: 10-24-1997 (971024) Publication Year: 1997
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: Reports
Word Count: 1989

(THIS IS THE FULLTEXT)

...Text: of cells in multicellular organisms requires continuous

stimulation from the extracellular environment. Certain growth factors maintain cell survival during embryonal and postnatal development (B4) . The **intracellular** signaling pathways by which growth factors promote survival are poorly understood. PI 3-kinase is recruited and activated during the **intracellular** signal transduction of many receptors and has been implicated in the signaling of survival factors (B5) . PI 3-kinase phosphorylates inositol lipids that act as...

...B9) and is activated by a variety of growth factors through a PI 3-kinase-dependent pathway (B6) (B7) . Activation of Akt is known to **deliver** a survival signal that inhibits the apoptosis induced by growth factor withdrawal in neurons, fibroblasts, and lymphoid cells (B10) (B11) . Activation of Akt ultimately leads... Stimulation of the PI 3-kinase-Akt signaling pathway through several growth factor receptors, including the IL-3 receptor, **delivers** a survival signal that ultimately leads to inhibition of apoptosis. The results presented herein identify the death agonist BAD as a substrate of Akt. The...

...its cytosolic sequestration by the tau form of 14-3-3 proteins and prevents its binding to the survival factor Bcl-x.inf(L) at ***intracellular*** membrane sites (B3) . Because BAD exerts its death-promoting effects by heterodimerizing with and inhibiting the death antagonist Bcl-x.inf(L), phosphorylation of BAD... membrane-anchored Bcl-x.inf(L), leading to increased cell survival. Thus, BAD phosphorylation by Akt is a mechanism by which growth factor receptors could **deliver** a survival signal that leads to the inhibition of apoptosis. However, these results do not rule out the possibility that Akt promotes cell survival by...

...identified as an oncogene in mice and is overexpressed in some human tumors (B17) . Because Bcl-2 and Bcl-x.inf(L) are known to ***deliver*** oncogenic signals that result in tumor development, these results suggest that active Akt promotes tumor development, at least in part, by acting on Bcl-2...

...BAD. (Middle) .sup(32)P-labeled BAD (P-BAD) from which quantitation was done (B18) . (Bottom) Immunoblot (Western blot) of the same membrane with polyclonal **antibody** to BAD (Santa Cruz), developed by enhanced chemiluminescence (Amersham). The results are representative of three independent experiments...

...or left untreated. Cells were lysed, and cell lysates were precleared with normal rabbit serum and protein A-Sepharose. Endogenous Akt was immunoprecipitated with polyclonal **antibody** specific for Akt, and immunocomplexes were collected with protein A-Sepharose and used in an in vitro kinase reaction using [(gamma) -.sup(32)P]ATP... is shown in the upper panel. Autoradiography of the original membrane is shown in the panel below. Immunoblots of the same membrane incubated with polyclonal ***antibody*** to BAD or to Akt are shown in the lower panels. (B) Fold induction of BAD phosphorylation induced by WT Akt (n = 3), Myr-Akt...

...B) 293T cells were transfected with active Akt (Myr) or kinase-deficient Akt (KD) HA-tagged constructs; after 24 hours, Akt was immunoprecipitated with monoclonal **antibody** to HA (Boehringer) and used in an in vitro kinase reaction (B6) with purified WT rBAD (WT) or mutant BAD with Ser.sup(112) and...

...in the upper panel. The original autoradiography is shown below. Active Akt was autophosphorylated as reported (B6) . Immunoblots of the same membrane incubated with polyclonal **antibody** to BAD or to Akt are shown in the lower panels. The results are representative of four independent experiments. The amount of rBAD phosphorylation observed...

References and Notes:

...thank T. F. Franke, M. Andjelkovich, and P. Tsichlis for reagents and R. Perez-Ballester, M. Benedict, and N. Inohara for valuable discussions and critical ***review*** of the manuscript. Supported in part by NIH grant CA-64556, the University of Michigan/Parke-Davis Fellowship Program (L.d.P.), a Spanish Ministry...

4/3,K/50 (Item 3 from file: 370)
DIALOG(R)File 370:Science
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00501315 (USE 9 FOR FULLTEXT)

Signaling in Plant-Microbe Interactions

Baker, Barbara; Zambryski, Patricia; Staskawicz, Brian; Dinesh-Kumar, S. P. B. Baker and S. P. Dinesh-Kumar are in the Department of Plant and Microbial Biology, University of California, Berkeley, CA 94720, and the Plant Gene Expression Center, Agricultural Research Service, U.S. Department of Agriculture, 800 Buchanan Street, Albany, CA 94710, USA. P. Zambryski and B. Staskawicz are in the Department of Plant and Microbial Biology, University of California, Berkeley, CA 94720, USA.

Science Vol. 276 5313 pp. 726

Publication Date: 5-02-1997 (970502) Publication Year: 1997

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Articles

Word Count: 6522

(THIS IS THE FULLTEXT)

...Text: defense mechanisms, combined with understanding of the complex ecology of real-world disease processes, can lead to more effective protection against plant pathogens. In this ***review*** we analyze plant pathogen interactions, including microbial strategies for pathogenesis and key elements of host responses (Figs. 1 and 2). We focus on studies using ...which confers resistance to the bacterial pathogen *Xanthomonas oryzae* pv. *oryzae* (B66). Xa21 encodes a putative transmembrane receptor with an extracellular LRR domain and an **intracellular** serine-threonine kinase domain. The Xa21 structure suggests an evolutionary link between LRR protein (Cf) and the Pto kinase. The fifth class includes the HM1...

...of Avr determinants is apparently based on the location of the relevant R gene partners. For example, the N product, which is predicted to be **intracellular**, may interact with the TMV replicase product in the cytoplasm (B69). As described previously, Avr gene products from extracellular pathogens are probably **delivered** directly into the plant cells through a hrp type III secretion pathway. In fact, avrPto, avrRpt2, and avrB of *P. syringae*, as well as avrBs3...can be blocked by diphenylene iodonium, an inhibitor of mammalian NADPH oxidase, which suggests that a similar system is required in plants (B89) (B90). Furthermore, **antibodies** to various mammalian NADPH oxidase components cross-react with plant proteins of similar size (B89) (B90). The rbohA gene product from rice is a homolog...

References and Notes:

...Jaffer, and V. Williamson for discussion and scanning electron micrographs of pathogens; the many colleagues who provided preprints, unpublished results, and critical comments for this ***review***; and C. Tobias for help in preparation of the Hrp secretion figure.

4/3,K/51 (Item 4 from file: 370)
DIALOG(R)File 370:Science

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00501314 (USE 9 FOR FULLTEXT)

Exploitation of Mammalian Host Cell Functions by Bacterial Pathogens

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Science Vol. 276 5313 pp. 718

Publication Date: 5-02-1997 (970502) Publication Year: 1997

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Articles

Word Count: 7193

(THIS IS THE FULLTEXT)

...Abstract: with host cells. Many host cell functions, including signal transduction pathways, cytoskeletal rearrangements, and vacuolar trafficking, are exploited, and these are the focus of this ***review***. A bonus of this work is that bacterial virulence factors are providing new tools to study various aspects of mammalian cell functions, in addition to ...

...Text: ***Intracellular*** Life of Bacterial Pathogens The theme of exploitation of host functions continues when bacterial pathogens become ***intracellular*** parasites. Nearly all invasive bacteria enter a membrane-bound vacuole as part of their invasion process, but their subsequent fates vary. Certain bacteria thrive within...and nonphagocytic cells by macropinocytosis. They often reside in the resulting large membrane-bound vacuoles (spacious phagosomes), and they express several gene products that enhance **intracellular** survival by neutralizing lysosomal killing mechanisms that are mediated, for example, by cationic peptides. Within epithelial cells, the *S. typhimurium* vacuole appears to be uncoupled...

...thereby avoiding the process of development into lysosomes. The vacuolar adenosine triphosphatase, which is responsible for acidifying vesicles, is not incorporated into the membranes of ***intracellular*** *M. avium*-containing vacuoles (B31) so that the vacuole is not acidified, a prerequisite for activation of several lysosomal degradative enzymes. Most lysosomal markers, including those that are **delivered** by a mannose-6-phosphate receptor, do not reach *Mycobacterium*-containing vacuoles. *Chlamydia trachomatis*, an obligate ***intracellular*** pathogen, resides within a vacuole that remains completely uncoupled from the main endocytic route. The chlamydial inclusion contains no specific vesicle markers, but acquires and...

...triphosphate that is pumped in from the host cell by an unknown mechanism. *Legionella pneumophila*, the causative agent of Legionnaires' disease, also inhabits a unique **intracellular** niche within a membrane-bound vacuole. It enters phagocytes by an unusual phagocytic mechanism called "coiling phagocytosis," during which a phagocyte pseudopod coils around the...

...associated with host endoplasmic reticulum. It appears that the *Legionella* vacuole fuses with the rough endoplasmic reticulum, probably by exploiting autophagy machinery to establish an **intracellular** niche favorable for its replication. Several bacterial genes including *icm* and *dotA* have been shown to be critical for **intracellular** survival and growth of *Legionella* (B34...

...a surface receptor that does not target the vacuole to become a lysosome. The development of new techniques, such as the isolation of vacuoles containing **intracellular** pathogens and the use of confocal microscopy to label vacuolar membranes, coupled with the identification of bacterial genes that mediate these processes, will yield information...

...Escape from the vacuole and cell-to-cell spread. Not all

*****intracellular***** bacteria remain within a vacuole. Shigella, Listeria, and Rickettsia rapidly gain access to the cytosol, where they replicate. In the case of Shigella, the bacterial...Generally, when *****intracellular***** bacteria have actively replicated inside the host cell, the cell dies, often by lysis. This releases the bacteria, which then either invade other cells or...

...B44) . This direct cell-to-cell spread allows dissemination within tissues while the bacteria remain sheltered from bactericidal cells or host components such as circulating *****antibodies***** or complement...

4/3,K/52 (Item 5 from file: 370)
DIALOG(R)File 370:Science
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00500244 (USE 9 FOR FULLTEXT)

Protective Effect of Rotavirus VP6-Specific IgA Monoclonal Antibodies That Lack Neutralizing Activity

Burns, John W.; Siadat-Pajouh, Majid; Krishnaney, Ajit A.; Greenberg, Harry B.

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Science Vol. 272 5258 pp. 104

Publication Date: 4-05-1996 (960405) Publication Year: 1996

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Reports

Word Count: 2409

(THIS IS THE FULLTEXT)

Text: Mucosal IgA is a secretory **antibody** that forms a first line of defense against many pathogens. It is synthesized as an oligomeric molecule that can be transported via transcytosis across certain...

...described an in vitro model in which transcytosing IgA molecules form complexes with certain viruses that have entered the cell and thereby inhibit viral replication *****intracellularly***** (B3) . To determine whether this can occur in vivo and whether non-neutralizing **antibodies** can mediate this **intracellular** effect, we studied the effects of IgA monoclonal *****antibodies***** (mAbs) on rotavirus infection in mice...

...surrounded by a second protein layer composed of VP6 (42 kD). VP6 makes up about 50% of the virion mass and is highly immunogenic; however, **antibody** to VP6 does not have neutralizing activity in vitro (B4) (B6) . Two viral proteins of the outermost protein coat, the viral hemagglutinin VP4 (85 to...

...VP7 (37 kD), have been directly implicated as targets of serotype-specific neutralization in vitro and protection in vivo (B6) . However, the presence of neutralizing **antibody** to rotavirus in serum may not correlate with protection (B7) (B8) , and in some studies of humans and animals, protection against rotavirus infection appears to...

...a library of IgA-secreting mAbs directed at several rotavirus proteins and evaluated them in the murine model of rotavirus infection (B8) (B9) (B11) . Monoclonal *****antibodies***** of the IgA isotype were generated to the murine rotavirus strains EC, EHP, or EW (B12) . A "backpack tumor" model (B13) was used for analysis...

...of histocompatible BALB/c mice. At the injection site, the mice secreted mAbs that were subsequently transported in the circulatory system. If the secreted IgA **antibody** molecules were oligomeric, they could be physiologically transcytosed to mucosal surfaces (B14)...

...A high-titer, serotype G3-specific, neutralizing, anti-VP7 IgG hybridoma, 4F8, was also included because investigators have reported that large amounts of serum-neutralizing **antibody** correlate with protection against subsequent rotavirus infection (B16) . Between 14 and 16 days after transplantation, when the tumors were visible and hybridoma-produced **antibodies** could be detected in sera and stools, the backpack mice were orally challenged with 10^{sup(4)} shedding dose 50s of wild-type EC murine...

...VP4, IgG mAbs to VP7, or IgG mAbs to VP6 were not protected from challenge (Fig. 1A and Table 1). However, two of three IgA *****antibodies***** to VP6 (7D9 and 10C10) completely blocked infection (Table 1 and Fig. 1A), whereas one IgA mAb to VP6 (8D3) had no effect. Four clonings of the 7D9 hybridoma did not alter its antiviral activity. The two positive **antibodies** to VP6 (7D9 and 10C10) were isolated from independent fusions. Both 7D9 and 10C10 react exclusively with the trimeric form of VP6 (B15) and neither...

...Fig. 2); however, the amount of IgA varied in different animals as previously described (B13) . Similar studies with IgA mAbs to VP4 demonstrated that these **antibodies** were also transported into the small intestine by the time of challenge (B15) . IgG mAbs were not detected in feces before challenge (B15) . The amount of IgA *****antibody***** in the feces at the time of challenge (Fig. 2) was less than or comparable to the amount seen after primary rotavirus infection, which indicatesTo determine if **antibody** was capable of resolving ongoing infection, BALB/c mice with severe combined immunodeficiency disease (SCID) were infected as sucklings with wild-type EW (G3P16) murine...

...of passively transferred IgA ascites to reduce illness in 5-day-old suckling mice. Intraperitoneal administration of 7D9 IgA ascites, but not of 8D3 control **antibody** (100 (mu) l per day for 7 days), delayed the onset and shortened the duration of diarrheal illness by 3 days in more than 50...

...We next carried out a passive feeding study with high-titer ascites (3 x 10^{sup(5)} dilution positive in ELISA) containing the 7D9 *****antibody***** or control ascites containing a non-neutralizing IgG mAb to VP7 (B17) . Feeding of 100 (mu) l of **antibody** 7D9 in ascites form did not alter the shedding of EC virus in three mice, indicating that orally administered mAb 7D9 to VP6 is not...

...7D9. No intestinal cell staining was observed when closed intestinal loops (B18) of mice were inoculated with EC virus mixed with high-titer IgG neutralizing **antibodies** to VP4 and VP7 (B15) , whereas loops inoculated with EC virus alone, with EC virus mixed with 7D9 mAb, or with EC plus IgA myeloma (an irrelevant **antibody**) all showed staining of rotavirus-infected intestinal epithelial cells (Fig. 4, A through C, respectively). On the other hand, isolated loops of small intestine in mice carrying 7D9 backpack tumors were fully resistant to primary infection with the EC strain of murine rotavirus (Fig. 4D) (B19) . Thus, IgA **antibody** was not able to inhibit primary rotavirus replication when

directly administered on the luminal side of the intestine, even at very high concentration, but was effective if **delivered** to isolated loops from the circulation...

...in the gut lumen. This conclusion is reinforced by the finding that transplantation of a mAb-secreting tumor that produced large amounts of neutralizing IgG **antibody** (4F8, Table 1) did not prevent or resolve rotavirus infection, presumably because the IgG **antibody** did not gain access to the gut lumen. Further studies with other mucosal pathogens are needed to determine the general applicability of this protective mechanism ...ELISA (B15) . Immunization with VP6-encoding DNA has also been shown to protect mice from rotavirus challenge in recent studies (B20) . If VP6-specific IgA **antibodies** with similar protective activity are generated after natural rotavirus infection or vaccination, they are likely to play a role in the heterotypic immunity observed in...

...Figure F1 Figure Removed

Figure F2

Caption: Presence of IgA **antibody** in stool of mice transplanted with the 7D9 hybridoma. Three rotavirus-naïve BALB/c mice were injected with 10^{sup}(6) 7D9 hybridoma cells as...

...immunostained for EC rotavirus. Approximately 1 cm of ileal loops were removed from mice after 12 hours of exposure to activated EC and to different *****antibodies***** as indicated and described (B18) . Four sections were obtained from each end and four from the middle portion of each loop. A total of 12...

...Vectastain ABC kit, Vector Laboratories, Burlingame, California). Loops were inoculated with (A) EC alone, (B) EC plus mAb 7D9, (C) EC plus mouse IgA (irrelevant **antibody**), and (D) EC alone in 7D9 backpack animals (magnification, x 400). Arrows indicate rotavirus-infected cells. All experiments carried out on animals were in accordance...

References and Notes:

...30. Supported by NIH grants R37AI21362 and DK38707, by a VA Merit *****Review***** grant, and by funds from the World Health Organization. H.B.G. is a VA Medical Investigator.

4/3,K/53 (Item 6 from file: 370)
DIALOG(R)File 370:Science
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00500185 (USE 9 FOR FULLTEXT)

A Permease-Oxidase Complex Involved in High-Affinity Iron Uptake in Yeast
Stearman, Robert; Yuan, Daniel S.; Yamaguchi-Iwai, Yuko; Klausner, Richard D.; Dancis, Andrew

Cell Biology and Metabolism Branch, National Institutes of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20892, USA.

Science Vol. 271 5255 pp. 1552

Publication Date: 3-15-1996 (960315) Publication Year: 1996

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Research Articles

Word Count: 3854

(THIS IS THE FULLTEXT)

...Text: oxidase, FET3, in iron uptake (B10) (B11) . Because the FET3 oxidase activity is required for iron uptake, copper deficiency or

mutations in genes involved in **delivery** of copper to FET3 abrogate iron uptake as a secondary effect. These genes include CTR1, the cellular copper uptake transporter (B10) , and CCC2, an **intracellular** copper transporter (B12) . The human multicopper oxidase ceruloplasmin exhibits similarity to the yeast FET3 oxidase (B11) . Ceruloplasmin plays an important role in human iron homeostasis...early in the secretory pathway, most likely in the ER. The complex progresses to a post-Golgi compartment (B39) , where the CCC2 protein mediates copper *****delivery***** to FET3. Finally, the copper-loaded FET3 protein, presumably still complexed to FTR1 protein, is **delivered** to the plasma membrane and becomes competent for iron transport. The point mutation in FTR1, altering a single glutamic acid residue of the REGLE motif...copper protein with an oxidase activity similar to that of FET3 (B11) . The P-type ATPase encoded by the Wilson disease gene is required to **deliver** copper to ceruloplasmin (B14) , analogous to the requirement for CCC2 (B15) in the **delivery** of copper to FET3 in yeast (B12) . Recently, mutations in the gene for human ceruloplasmin have been identified that result in a neurologic syndrome attributed...FTR1 with MYC tag) (B36) and 352FET3; (C and D) 702FTR1myc and YEp352. The transformants were grown in iron-depleted medium, fixed, and stained with **antibodies** to the MYC epitope (A to C) or with DAPI (D). Bar, 10 (mu) m...

References and Notes:

...in vitro studies of the proton-pumping ATPase of erythrocytes [C. Li, J. A. Watkins, J. Glass, J. Biol. Chem. 269, 10242 (1994)]. For a *****review***** of human iron metabolism, see G. M. Brittenham, in Hematology, Basic Principles and Practice, R. Hoffman et al., Eds. (Churchill Livingstone, New York, 1995), pp...S. Dietrich for providing sequence information from the S. cerevisiae genome project before publication; J. Bonifacino, T. Rouault, G. Storz, and J. Stubbe for critical **review** of the manuscript and helpful conversations and comments; and N. Brun and J. Kelly for assisting

4/3,K/54 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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141121938 CA: 141(8)121938a JOURNAL
Intracellular targeting of antibodies in mammalian cells
AUTHOR(S): Zhu, Quan; Marasco, Wayne A.
LOCATION: Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute; Department of Medicine, Harvard Medical School, Boston, MA, 02115, USA
JOURNAL: New Compr. Biochem. (New Comprehensive Biochemistry) DATE: 2003
VOLUME: 38, PAGES: 573-587 CODEN: NCBIDL ISSN: 0167-7306 LANGUAGE: English PUBLISHER: Elsevier Science B.V.

4/3,K/55 (Item 1 from file: 50)

DIALOG(R)File 50:CAB Abstracts

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0007562780 CAB Accession Number: 19980403801

Lactic acid bacteria as a vaccine delivery vehicle: a *****review***** .
Yoon, Y. H.
Department of Animal Science, Chung-Ang University, Ansung 456-756, Korea Republic.
Korean Journal of Dairy Science vol. 19 (4): p.379-388
Publication Year: 1997
ISSN: 0253-2980
Language: Korean Summary Language: English Record Type: Abstract

Document Type: Journal article

Lactic acid bacteria as a vaccine delivery vehicle: a ***review***

Oral administration of recombinant lactic acid bacteria can be used to elicit local IgA or serum IgG **antibody** responses to an expressed antigen. It is not clear to what extent the antigen expressed by the different recombinant lactic acid bacteria and the amount...

... responses via mucosal routes of immunization. It would be of considerable interest to compare the immune responses to a model antigen when it is expressed **intracellularly**, secreted or displayed on the surface of lactic acid bacteria which are being developed as vaccine ***delivery*** vehicles. This establishes the relative importance of colonization in eliciting an immune response and the influence of the mucosal site of colonization on the magnitude...

... effects of lactic acid bacteria and their interaction with hosts will help to identify strains which are most beneficial and suitable for the different vaccine ***delivery*** systems under development. To date, the results are very encouraging as they indicate that lactic acid bacteria are capable of **delivering** antigen to antigen presenting cells of the mucosal and systemic immune systems following oral immunization.

4/3,K/56 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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02237569 SUPPLIER NUMBER: 106143270 (USE FORMAT 7 OR 9 FOR FULL TEXT)
)

Molecular imaging of cancer: the basics. (CE Directed Reading).

Furlow, Bryant

Radiologic Technology, 74, 6, 486(15)

July-August,

2003

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0033-8397

LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:

Academic; Professional; Trade

WORD COUNT: 7890 LINE COUNT: 00721

... particular cells. In the case of therapeutic gene insertion into a diseased genome, reporter genes can be attached to the therapeutic genes before they are ***delivered*** into their cellular targets. Reporter genes encode **intracellular** enzymes or proteins that appear on the cell's surface, such as ***antibody*** -binding cell surface receptors. For example, genetically engineered receptors have been created that bind to approved PET imaging agents, such as perrhenate.

When the gene...

...specific antigen relapse after treatment for localized prostate cancer.

J Urol. 1999;162:1322-1328.

(10.) Kubota K. From tumor biology to clinical PET: a ***review*** of positron emission tomography (PET) in oncology. Ann Nucl Med. 2001;15:471-486.

(11.) Vranjesevic D, Filmont JE, Meta J, et al. Whole-body...

4/3,K/57 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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02099714 SUPPLIER NUMBER: 90098057 (USE FORMAT 7 OR 9 FOR FULL TEXT)

20 Poisoning-induced nephrotoxicity.

Vale, JA

Journal of Toxicology: Clinical Toxicology, 40, 3, 264(4)

April,

2002

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0731-3810

LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional

WORD COUNT: 2485 LINE COUNT: 00216

TEXT:

Definition: This **review** will focus on the development of adverse alterations in renal structure or function occurring in the setting of acute or chronic poisoning. Nephrotoxicity appearing during...

...some 22% of the cardiac output (about 1 100mL/min). This substantial blood flow ensures, firstly, that large quantities of oxygen and metabolic substrates are **delivered** to the kidneys to maintain function and, secondly, that sufficient plasma is available for the high rates of glomerular filtration that are necessary to preserve...

...addition, because of the considerable renal blood supply, especially to the cortex which receives about 80% of the total renal blood flow, circulating poisons are *****delivered***** to the kidneys in large amount. As many poisons undergo active transport from the blood into proximal tubular cells and then diffuse into the tubular...

...as the poison passes down the nephron into the medulla, producing a concentration of poison many times greater than that in the plasma, leading to *****intracellular***** toxicity. Mechanisms of toxicity: Each part of the nephron can be perturbed by a nephrotoxic insult. Pathogenic mechanisms include direct cytotoxicity, where the effect is...

...due to hemorrhage or corrosive damage, and the loss of tissue fluid, for example from a large chemical burn. Illustrative examples: Paracetamol (Acetaminophen): In a **review** of 2060 unselected patients poisoned with paracetamol and treated over the period 1969-1980, the overall frequency of acute renal failure was 1.6 per...tubular acidosis, have been reported following volatile substance abuse, particularly with toluene. An immune-complex type of glomerulonephritis, particularly anti-glomerular basement membrane (anti-GBM) **antibody**-mediated diseases, such as Goodpasture's syndrome, can follow relatively low-level exposure to a wide variety of hydrocarbons. Studies in patients with glomerulonephritis, and ...Ann. Clin. Biochem. 1994, 31, 331-334. (8.) Jones, G.M.; Vale, J.A. Mechanisms of Toxicity, Clinical Features, and Management of Diquat Poisoning: A *****Review*****. J. Toxicol. Clin. Toxicol. 2000, 38, 123-128. (9.) Poldelski, V.; Johnson, A.; Wright, S.; Dela Rosa, V.; Zager, R.A. Ethylene Glycol-Mediated Tubular...

4/3,K/58 (Item 3 from file: 149)

DIALOG(R)File 149:TGG Health&Wellness DB(SM)

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01150667 SUPPLIER NUMBER: 06914062 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Living with clathrin: its role in intracellular membrane traffic.

Brodsky, Frances M.

Science, v242, n4884, p1396(7)

Dec 9,

1988

PUBLICATION FORMAT: Magazine/Journal ISSN: 0036-8075 LANGUAGE: English

RECORD TYPE: Fulltext TARGET AUDIENCE: Academic

WORD COUNT: 4358 LINE COUNT: 00446

MOVEMENT OF MEMBRANE-BOUND AND SECRETED PROTEINS to and from the plasma membrane and between **intracellular** membrane compartments requires budding and fusion of membrane vesicles. For more than 10 years,

cell biologists have been investigating molecular interactions that regulate this process of *****intracellular***** membrane traffic. The protein clathrin was first identified as a participant when Pearse purified it from coated vesicles isolated from pig brain. Recent advances in the characterization of clathrin include the cloning and sequencing of DNA coding for the clathrin subunits and the production of monoclonal *****antibodies***** (MAbs) to clathrin. This progress made it possible to examine clathrin's role in **intracellular** traffic by production of yeast mutants lacking clathrin and by cytoplasmic **delivery** of MAbs to clathrin. Although these studies initially generated controversy about clathrin function, they have helped formulate a more precise conception of how clathrin participates in membrane transport. This *****review***** will summarize the recent insights into the structure of clathrin and the formation of coated vesicles as well as the experiments that have led to...

...of the yeast mutants should resolve these questions as well as provide clues about the function of clathrin in other organisms.

Clathrin function in mammalian **intracellular** transport was examined after bulk **delivery** of high concentrations of **antibody** to clathrin into the cytoplasm of CV-1 monkey kidney cells. This procedure reduced endocytic activity by 50%. Results indicated that clathrin participates actively in...

...experiment in which microinjection of immunoglobulin from clathrin antiserum had no effect on receptor uptake is not necessarily contradictory, since inhibition of clathrin assembly with **antibodies** is quite sensitive to the concentration and specificity of the

*****antibodies*****. In fact, incomplete inhibition of endocytosis in the CV-1 cells might be explained by variations in the **antibody** concentrations

*****delivered***** to individual cells. Alternatively, some endocytosis may occur through a pathway in which clathrin is not involved. For cells receiving MAbs to clathrin in concentrations...is controlled by endocytosis, followed by recycling, degradation, or transcytosis. Clathrin-mediated internalization facilitates this process by concentrating receptors and increasing the efficiency of their **delivery** to endosomes where they are sorted into different **intracellular** pathways. Endocytosis caused by noncoated membrane invagination **delivers** internalized ligands and receptors to endosomes in a less efficient manner than clathrin-mediated uptake and may suffice as a default pathway of internalization with...

...provided by clathrin. There are five documented exceptions, in contrast to the more than 20 different receptors that have been observed in clathrin-coated pits. *****Antibody***** to the "excluded" receptor Thy1 causes capping, which suggests that these receptors are actively retained on the cell surface or that nonselective membrane invagination does not contribute substantially to endocytosis in the particular cells studied. Excluded Class I histocompatibility molecules have been observed in noncoated membrane invaginations after treatment with **antibody**, but the efficiency of their internalization is poor.

Attempts to define the molecular signals responsible for receptor uptake in clathrin-coated pits have implicated positive...